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APPLICATION NUMBER: ***60/548,789***
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THE COUNTRY CODE AND NUMBER OF YOUR PRIORITY APPLICATION, TO BE USED FOR FILING ABROAD UNDER THE PARIS CONVENTION, IS ***US60/548,789***

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PROVISIONAL APPLICATION FOR PATENT COVER SHEET

This is a request for filing a PROVISIONAL APPLICATION FOR PATENT under 37 CFR 1.53(c).

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INVENTOR(S)

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Additional inventors are being named on the second *separately numbered sheets attached hereto*

TITLE OF THE INVENTION (500 characters max)

Immunogenic Compositions For Streptococcus Agalactiae

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ENCLOSED APPLICATION PARTS *(check all that apply)*

☑ Specification *Number of Pages* 53 ☐ CD(s), Number

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☐ Application Data Sheet. See 37 CFR 1.76

METHOD OF PAYMENT OF FILING FEES FOR THIS PROVISIONAL APPLICATION FOR PATENT

☐ Applicant claims small entity status. See 37 CFR 1.27.

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Respectfully submitted,

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Date February 26, 2004

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Additional Page

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Docket Number 20665.001

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Number 2 of 2

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IMMUNOGENIC COMPOSITIONS FOR *STREPTOCOCCUS AGALACTIAE*

This application incorporates by reference in its entirety International Patent Application No. PCT/US03/29167, Attorney Reference No. PP19766.002, filed on September 15, 2003.

FIELD OF THE INVENTION

The invention relates to an immunogenic antigen derived from *Streptococcus agalactiae* ("GBS") and its use in synergistic combinations with other GBS antigens. In particular, the invention relates to a composition comprising a combination of two or more GBS antigens, wherein the combination includes GBS 80 or a fragment thereof. In one embodiment, the combination may consist of two to thirteen GBS antigens selected from an antigen group consisting of GBS 80, GBS 91, GBS 104, GBS 184, GBS 276, GBS 305, GBS 322, GBS 330, GBS 338, GBS 361, GBS 404, GBS 690, and GBS 691. Preferably, the combination includes GBS 80 in combination with one or more of GBS 104 and GBS 322.

BACKGROUND OF THE INVENTION

GBS has emerged in the last 20 years as the major cause of neonatal sepsis and meningitis that affect 0.5 – 3 per 1000 live births, and an important cause of morbidity among the older age group affecting 5 – 8 per 100,000 of the population. Current disease management strategies rely on intrapartum antibiotics and neonatal monitoring which have reduced neonatal case mortality from >50% in the 1970's to less than 10% in the 1990's. Nevertheless, there is still considerable morbidity and mortality and the management is expensive. 15 – 35% of pregnant women are asymptomatic carriers and at high risk of transmitting the disease to their babies. Risk of neonatal infection is associated with low serotype specific maternal antibodies and high titers are believed to be protective. In addition, invasive GBS disease is increasingly recognized in elderly adults with underlying disease such as diabetes and cancer.

The "B" in "GBS" refers to the Lancefield classification, which is based on the antigenicity of a carbohydrate which is soluble in dilute acid and called the C carbohydrate. Lancefield identified 13 types of C carbohydrate, designated A to O, that could be serologically differentiated. The organisms that most commonly infect humans are found in groups A, B, D, and G. Within group B, strains can be divided into at least 9 serotypes (Ia, Ib, Ia/c, II, III, IV, V, VI, VII and VIII) based on the structure of their polysaccharide capsule. In the past, serotypes Ia, Ib, II, and III were equally prevalent in normal vaginal carriage and early onset sepsis in newborns. Type V GBS has emerged as an important cause of GBS infection in the USA, however, and strains of types VI and VIII have become prevalent among Japanese women.

The genome sequence of a serotype V strain 2603 V/R has been published (Ref. 1) and various polypeptides for use a vaccine antigens have been identified (Ref. 2). The vaccines currently in clinical trials, however, are based on polysaccharide antigens. These suffer from serotype-specificity and poor immunogenicity, and so there is a need for effective vaccines against *S.agalactiae* infection.

It is an object of the invention to provide further and improved compositions for providing immunity against GBS disease and/or infection. The compositions are based on a combination of two or more (e.g., three or more) GBS antigens.

SUMMARY OF THE INVENTION

Applicants have discovered that an immunogenic GBS antigen, GBS 80, is particularly suitable for immunization purposes, especially when used in synergistic combinations with other GBS antigens. In particular, the invention relates to a composition comprising a combination of two or more GBS antigens, wherein the combination includes GBS 80 or a fragment thereof. In one embodiment, the combination may consist of two to thirteen GBS antigens selected from the group consisting of GBS 80, GBS 91, GBS 104, GBS 184, GBS 276, GBS 305, GBS 322, GBS 330, GBS 338, GBS 361, GBS 404, GBS 690, and GBS 691. Preferably, the combination consists of GBS 80, GBS 104 and GBS 322.

Instead of the full length antigen, the combination may comprise an immunogenic fragment of the selected GBS antigen and/or a polypeptide sequence having sequence identity to the selected antigen.

Preferably, the combination of GBS antigens consists of three, four, five, six, seven, eight, nine, or ten GBS antigens. Still more preferably, the combination of GBS antigens consists of three, four, or five GBS antigens.

DETAILED DESCRIPTION OF THE INVENTION

The practice of the present invention will employ, unless otherwise indicated, conventional methods of chemistry, biochemistry, molecular biology, immunology and pharmacology, within the skill of the art. Such techniques are explained fully in the literature. See, e.g., *Remington's Pharmaceutical Sciences*, Mack Publishing Company, Easton, Pa., 19th Edition (1995); *Methods In Enzymology* (S. Colowick and N. Kaplan, eds., Academic Press, Inc.); and *Handbook of Experimental Immunology*, Vols. I-IV (D.M. Weir and C.C. Blackwell, eds., 1986, Blackwell Scientific Publications); Sambrook, et al., *Molecular Cloning: A Laboratory Manual* (2nd Edition, 1989); *Handbook of Surface and Colloidal Chemistry* (Birdi, K.S. ed., CRC Press, 1997); *Short Protocols in Molecular Biology*, 4th ed. (Ausubel et al. eds., 1999, John Wiley & Sons); *Molecular Biology Techniques: An Intensive Laboratory Course*, (Ream et al., eds., 1998, Academic Press); *PCR (Introduction to Biotechniques Series)*, 2nd ed. (Newton & Graham eds., 1997, Springer Verlag); Peters and Dalrymple, *Fields Virology* (2d ed), Fields et al. (eds.), B.N. Raven Press, New York, NY.

All publications, patents and patent applications cited herein, are hereby incorporated by reference in their entireties.

GBS Antigens

As discussed above, the invention provides an immunogenic composition comprising a combination of two or more GBS antigens, wherein said combination includes GBS 80 or a fragment thereof.

The combinations of GBS antigens may include polypeptide fragments of the identified GBS antigens. The length of the fragment may vary depending on the amino acid sequence of the specific GBS antigen, but the fragment is preferably at least 7 consecutive amino acids, (*e.g.* 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200 or more). Preferably the fragment comprises one or more epitopes from the sequence. Other preferred fragments include (1) the N-terminal signal peptides of each identified GBS antigen, (2) the identified GBS antigens without their N-terminal signal peptides, and (3) each identified GBS antigen wherein up to 10 amino acid residues (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) are deleted from the N-terminus and/or the C-terminus *e.g.* the N-terminal amino acid residue may be deleted. Other fragments omit one or more domains of the protein (*e.g.* omission of a signal peptide, of a cytoplasmic domain, of a transmembrane domain, or of an extracellular domain).

The combinations of GBS antigens may include polypeptide sequences having sequence identity to the identified GBS antigens. The degree of sequence identity may vary depending on the amino acid sequence (a) in question, but is preferably greater than 50% (*e.g.* 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more). Polypeptides having sequence identity include homologs, orthologs, allelic variants and functional mutants of the identified GBS antigens. Typically, 50% identity or more between two proteins is considered to be an indication of functional equivalence. Identity between proteins is preferably determined by the Smith-Waterman homology search algorithm as implemented in the MPSRCH program (Oxford Molecular), using an affinity gap search with parameters *gap open penalty=12* and *gap extension penalty=1*.

The polypeptides can, of course, be prepared by various means (*e.g.* recombinant expression, purification from GBS, chemical synthesis *etc.*) and in various forms (*e.g.* native, fusions, glycosylated, non-glycosylated *etc.*). They are preferably prepared in substantially pure form (*i.e.* substantially free from other streptococcal or host cell proteins) or substantially isolated form.

GBS 80

As discussed above, the invention relates to the use of GBS 80 in synergistic combination with other GBS antigens. GBS 80 refers to a putative cell wall surface anchor family protein. Nucleotide and amino acid sequence of GBS 80 sequenced from serotype V isolated strain 2603 V/R are set forth in Ref. 3 as SEQ ID 8779 and SEQ ID 8780. These sequences are also set forth below as SEQ ID NOS 1 and 2:

SEQ ID NO. 1

ATGAAATTATCGAAGAAGTTATTGTTTTCGGCTGCTGTTTTAACAATGGTGGCGGGGTCAACTGTTGAACCA
GTAGCTCAGTTTGCGACTGGAATGAGTATTGTAAGAGCTGCAGAAGTGTCACAAGAACGCCCAGCGAAAACA
ACAGTAAATATCTATAAATTACAAGCTGATAGTTATAAATCGGAAATTACTTCTAATGGTGGTATCGAGAAT
AAAGACGGCGAAGTAATATCTAACTATGCTAAACTTGGTGACAATGTAAAAGGTTTGCAAGGTGTACAGTTT
AAACGTTATAAAGTCAAGACGGATATTTCTGTTGATGAATTGAAAAAATTGACAACAGTTGAAGCAGCAGAT
GCAAAAGTTGGAACGATTCTTGAAGAAGGTGTCAGTCTACCTCAAAAAACTAATGCTCAAGGTTTGGTCGTC
GATGCTCTGGATTCAAAAAGTAATGTGAGATACTTGTATGTAGAAGATTTAAAGAATTCACCTTCAAACATT
ACCAAAGCTTATGCTGTACCGTTTGTGTTGGAATTACCAGTTGCTAACTCTACAGGTACAGGTTTCCTTTCT
GAAATTAATATTTACCCTAAAAACGTTGTAACTGATGAACCAAAAACAGATAAAGATGTTAAAAAATTAGGT
CAGGACGATGCAGGTTATACGATTGGTGAAGAATTCAAATGGTTCTTGAAATCTACAATCCCTGCCAATTTA
GGTGACTATGAAAAATTTGAAATTACTGATAAATTTGCAGATGGCTTGACTTATAAATCTGTTGGAAAAATC
AAGATTGGTTCGAAAACACTGAATAGAGATGAGCACTACACTATTGATGAACCAACAGTTGATAACCAAAAT

ACATTAAAAATTACGTTTAAACCAGAGAAATTTAAAGAAATTGCTGAGCTACTTAAAGGAATGACCCTTGTT
AAAAATCAAGATGCTCTTGATAAAGCTACTGCAAATACAGATGATGCGGCATTTTTGGAAATTCCAGTTGCA
TCAACTATTAATGAAAAAGCAGTTTTAGGAAAAGCAATTGAAAATACTTTTGAACTTCAATATGACCATACT
CCTGATAAAGCTGACAATCCAAAACCATCTAATCCTCCAAGAAAACCAGAAGTTCATACTGGTGGGAAACGA
TTTGTAAAGAAAGACTCAACAGAAACACAAACACTAGGTGGTGCTGAGTTTGATTTGTTGGCTTCTGATGGG
ACAGCAGTAAAATGGACAGATGCTCTTATTAAAGCGAATACTAATAAAAACTATATTGCTGGAGAAGCTGTT
ACTGGGCAACCAATCAAATTGAAATCACATACAGACGGTACGTTTGAGATTAAAGGTTTGGCTTATGCAGTT
GATGCGAATGCAGAGGGTACAGCAGTAACTTACAAATTAAAAGAAACAAAAGCACCAGAAGGTTATGTAATC
CCTGATAAAGAAATCGAGTTTACAGTATCACAAACATCTTATAATACAAAACCAACTGACATCACGGTTGAT
AGTGCTGATGCAACACCTGATACAATTAAAAACAACAAACGTCCTTCAATCCCTAATACTGGTGGTATTGGT
ACGGCTATCTTTGTCGCTATCGGTGCTGCGGTGATGGCTTTTGCTGTTAAGGGGATGAAGCGTCGTACAAAA
GATAAC

SEQ ID NO: 2

MKLSKKLLFSAAVLTMVAGSTVEPVAQFATGMSIVRAAEVSQERPAKTTVNIYKLQADSYKSEITSNGGIEN
KDGEVISNYAKLGDNVKGLQGVQFKRYKVKTDISVDELKKLTTVEAADAKVGTILEEGVSLPQKTNAQGLVV
DALDSKSNVRYLYVEDLKNSPSNITKAYAVPFVLELPVANSTGTGFLSEINIYPKNVVTDEPKTDKDVKKLG
QDDAGYTIGEEFKWFLKSTIPANLGDYEKFEITDKFADGLTYKSVGKIKIGSKTLNRDEHYTIDEPTVDNQN
TLKITFKPEKFKEIAELLKGMTLVKNQDALDKATANTDDAAFLEIPVASTINEKAVLGKAIENTFELQYDHT
PDKADNPKPSNPPRKPEVHTGGKRFVKKDSTETQTLGGAEFDLLASDGTAVKWTDALIKANTNKNYIAGEAV
TGQPIKLKSHTDGTFEIKGLAYAVDANAEGTAVTYKLKETKAPEGYVIPDKEIEFTVSQTSYNTKPTDITVD
SADATPDTIKNNKRPS*IPNT*GGIGTAIFVAIGAAVMAFAVKGMKRRTKDN

As described above, the combinations of the invention may include a fragment of a GBS antigen. In some instances, removal of one or more domains, such as a leader or signal sequence region, a transmembrane region, a cytoplasmic region or a cell wall anchoring motif, may facilitate cloning of the gene encoding the antigen and/or recombinant expression of the GBS protein. In addition, fragments comprising immunogenic epitopes of the cited GBS antigens may be used in the compositions of the invention.

GBS 80 contains an N-terminal leader or signal sequence region which is indicated by the underlined sequence at the beginning of SEQ ID NO: 2 above. In one embodiment, one or more amino acids from the leader or signal sequence region of GBS 80 are removed. An example of such a GBS 80 fragment is set forth below as SEQ ID NO: 3:

SEQ ID NO: 3

AEVSQERPAKTTVNIYKLQADSYKSEITSNGGIENKDGEVISNYAKLGDNVKGLQGVQFKRYKVKTDISVDE
LKKLTTVEAADAKVGTILEEGVSLPQKTNAQGLVVDALDSKSNVRYLYVEDLKNSPSNITKAYAVPFVLELP
VANSTGTGFLSEINIYPKNVVTDEPKTDKDVKKLGQDDAGYTIGEEFKWFLKSTIPANLGDYEKFEITDKFA
DGLTYKSVGKIKIGSKTLNRDEHYTIDEPTVDNQNTLKITFKPEKFKEIAELLKGMTLVKNQDALDKATANT
DDAAFLEIPVASTINEKAVLGKAIENTFELQYDHTPDKADNPKPSNPPRKPEVHTGGKRFVKKDSTETQTLG
GAEFDLLASDGTAVKWTDALIKANTNKNYIAGEAVTGQPIKLKSHTDGTFEIKGLAYAVDANAEGTAVTYKL
KETKAPEGYVIPDKEIEFTVSQTSYNTKPTDITVDSADATPDTIKNNKRPSIPNTGGIGTAIFVAIGAAVMA
FAVKGMKRRTKDN

GBS 80 contains a C-terminal transmembrane region which is indicated by the underlined sequence near the end of SEQ ID NO: 2 above. In one embodiment, one or more amino acids from the transmembrane region and/or a cytoplasmic region are removed. An example of such a GBS 80 fragment is set forth below as SEQ ID NO: 4:

SEQ ID NO: 4

MKLSKKLLFSAAVLTMVAGSTVEPVAQFATGMSIVRAAEVSQERPAKTTVNIYKLQADSYKSEITSNGGIEN
KDGEVISNYAKLGDNVKGLQGVQFKRYKVKTDISVDELKKLTTVEAADAKVGTILEEGVSLPQKTNAQGLVV
DALDSKSNVRYLYVEDLKNSPSNITKAYAVPFVLELPVANSTGTGFLSEINIYPKNVVTDEPKTDKDVKKLG
QDDAGYTIGEEFKWFLKSTIPANLGDYEKFEITDKFADGLTYKSVGKIKIGSKTLNRDEHYTIDEPTVDNQN
TLKITFKPEKFKEIAELLKGMTLVKNQDALDKATANTDDAAFLEIPVASTINEKAVLGKAIENTFELQYDHT
PDKADNPKPSNPPRKPEVHTGGKRFVKKDSTETQTLGGAEFDLLASDGTAVKWTDALIKANTNKNYIAGEAV
TGQPIKLKSHTDGTFEIKGLAYAVDANAEGTAVTYKLKETKAPEGYVIPDKEIEFTVSQTSYNTKPTDITVD
SADATPDTIKNNKRPS*IPNTG*

GBS 80 contains an amino acid motif indicative of a cell wall anchor: **SEQ ID NO: 5** IPNTG (shown in italics in SEQ ID NO: 2 above). In some recombinant host cell systems, it may be preferable to remove this motif to facilitate secretion of a recombinant GBS 80 protein from the host cell. Accordingly, in one preferred fragment of GBS 80 for use in the invention, the transmembrane and/or cytoplasmic regions and the cell wall anchor motif are removed from GBS 80. An example of such a GBS 80 fragment is set forth below as SEQ ID NO: 6.

SEQ ID NO: 6
MKLSKKLLFSAAVLTMVAGSTVEPVAQFATGMSIVRAAEVSQERPAKTTVNIYKLQADSYKSEITSNGGIEN
KDGEVISNYAKLGDNVKGLQGVQFKRYKVKTDISVDELKKLTTVEAADAKVGTILEEGVSLPQKTNAQGLVV
DALDSKSNVRYLYVEDLKNSPSNITKAYAVPFVLELPVANSTGTGFLSEINIYPKNVVTDEPKTDKDVKKLG
QDDAGYTIGEEFKWFLKSTIPANLGDYEKFEITDKFADGLTYKSVGKIKIGSKTLNRDEHYTIDEPTVDNQN
TLKITFKPEKFKEIAELLKGMTLVKNQDALDKATANTDDAAFLEIPVASTINEKAVLGKAIENTFELQYDHT
PDKADNPKPSNPPRKPEVHTGGKRFVKKDSTETQTLGGAEFDLLASDGTAVKWTDALIKANTNKNYIAGEAV
TGQPIKLKSHTDGTFEIKGLAYAVDANAEGTAVTYKLKETKAPEGYVIPDKEIEFTVSQTSYNTKPTDITVD
SADATPDTIKNNKRPS

Alternatively, in some recombinant host cell systems, it may be preferable to use the cell wall anchor motif to anchor the recombinantly expressed protein to the cell wall. The extracellular domain of the expressed protein may be cleaved during purification or the recombinant protein may be left attached to either inactivated host cells or cell membranes in the final composition.

In one embodiment, the the leader or signal sequence region, the transmembrane and cytoplasmic regions and the cell wall anchor motif are removed from the GBS 80 sequence. An example of such a GBS 80 fragment is set forth below as SEQ ID NO: 7.

SEQ ID NO: 7
AEVSQERPAKTTVNIYKLQADSYKSEITSNGGIENKDGEVISNYAKLGDNVKGLQGVQFKRYKVKTDISVDE
LKKLTTVEAADAKVGTILEEGVSLPQKTNAQGLVVDALDSKSNVRYLYVEDLKNSPSNITKAYAVPFVLELP
VANSTGTGFLSEINIYPKNVVTDEPKTDKDVKKLGQDDAGYTIGEEFKWFLKSTIPANLGDYEKFEITDKFA
DGLTYKSVGKIKIGSKTLNRDEHYTIDEPTVDNQNTLKITFKPEKFKEIAELLKGMTLVKNQDALDKATANT
DDAAFLEIPVASTINEKAVLGKAIENTFELQYDHTPDKADNPKPSNPPRKPEVHTGGKRFVKKDSTETQTLG
GAEFDLLASDGTAVKWTDALIKANTNKNYIAGEAVTGQPIKLKSHTDGTFEIKGLAYAVDANAEGTAVTYKL
KETKAPEGYVIPDKEIEFTVSQTSYNTKPTDITVDSADATPDTIKNNKRPS

Applicants have identified a particularly immunogenic fragment of the GBS 80 protein. This immunogenic fragment is located towards the N-terminus of the protein and is underlined in the GBS 80 SEQ ID NO: 2 sequence below. The underlined fragment is set forth below as SEQ ID NO: 8.

SEQ ID NO: 2
MKLSKKLLFSAAVLTMVAGSTVEPVAQFATGMSIVRAAEVSQERPAKTTVNIYKLQADSYKSEITSNGGIEN
KDGEVISNYAKLGDNVKGLQGVQFKRYKVKTDISVDELKKLTTVEAADAKVGTILEEGVSLPQKTNAQGLVV
DALDSKSNVRYLYVEDLKNSPSNITKAYAVPFVLELPVANSTGTGFLSEINIYPKNVVTDEPKTDKDVKKLG

QDDAGYTIGEEFKWFLKSTIPANLGDYEKFEITDKFADGLTYKSVGKIKIGSKTLNRDEHYTIDEPTVDNQN
TLKITFKPEKFKEIAELLKGMTLVKNQDALDKATANTDDAAFLEIPVASTINEKAVLGKAIENTFELQYDHT
PDKADNPKPSNPPRKPEVHTGGKRFVKKDSTETQTLGGAEFDLLASDGTAVKWTDALIKANTNKNYIAGEAV
TGQPIKLKSHTDGTFEIKGLAYAVDANAEGTAVTYKLKETKAPEGYVIPDKEIEFTVSQTSYNTKPTDITVD
SADATPDTIKNNKRPS*IPNT*GGIGTAIFVAIGAAVMAFAVKGMKRRTKDN

SEQ ID NO: 8
AEVSQERPAKTTVNIYKLQADSYKSEITSNGGIENKDGEVISNYAKLGDNVKGLQGVQFKRYKVKTDISVDE
LKKLTTVEAADAKVGTILEEGVSLPQKTNAQGLVVDALDSKSNVRYLYVEDLKNSPSNITKAYAVPFVLELP
VANSTGTGFLSEINIYPKNVVTDEPKTDKDVKKLGQDDAGYTIGEEFKWFLKSTIPANLGDYEKFEITDKFA
DGLTYKSVGKIKIGSKTLNRDEHYTIDEPTVDNQNTLKITFKPEKFKEIAELLKG

The immunogenicity of the protein encoded by SEQ ID NO: 7 was compared against PBS, GBS whole cell, GBS 80 (full length) and another fragment of GBS 80, located closer to the C-terminus of the peptide (SEQ ID NO: 9, below).

SEQ ID NO: 9
MTLVKNQDALDKATANTDDAAFLEIPVASTINEKAVLGKAIENTFELQYDHTPDKADNPKPSNPPRKPEVHTGGKRFVKK
DSTETQTLGGAEFDLLASDGTAVKWTDALIKANTNKNYIAGEAVTGQPIKLKSHTDGTFEIKGLAYAVDANAEGTAVTYK
LKETKAPEGYVIPDKEIEFTVSQTSYNTKPTDITVDSADATPDTIKNNKRPS

Both an Active Maternal Immunization Assay and a Passive Maternal Immunization Assay were conducted on this collection of proteins.

As used herein, an Active Maternal Immunization assay refers to an *in vivo* protection assay where female mice are immunized with the test antigen composition. The female mice are then bred and their pups are challenged with a lethal dose of GBS. Serum titers of the female mice during the immunization schedule are measured as well as the survival time of the pups after challenge.

Specifically, the Active Maternal Immunization assays referred to herein used groups of four CD-1 female mice (Charles River Laboratories, Calco Italy). These mice were immunized intraperitoneally with the selected proteins in Freund's adjuvant at days 1, 21 and 35, prior to breeding. 6-8 weeks old mice received 20 µg protein/dose when immunized with a single antigen, 30-45 µg protein/dose (15 µg each antigen) when immunized with combination of antigens. The immune response of the dams was monitored by using serum samples taken on day 0 and 49. The female mice were bred 2-7 days after the last immunization (at approximately t= 36 – 37), and typically had a gestation period of 21 days. Within 48 hours of birth, the pups were challenged via I.P. with GBS in a dose approximately equal to a amount which would be sufficient to kill 70 – 90 % of unimmunized pups (as determined by empirical data gathered from PBS control groups). The GBS challenge dose is preferably administered in 50µl of THB medium. Preferably, the pup challenge takes place at 56 to 61 days after the first immunization. The challenge inocula were prepared starting from frozen cultures diluted to the appropriate concentration with THB prior to use. Survival of pups was monitored for 5 days after challenge.

As used herein, the Passive Maternal Immunization Assay refers to an *in vivo* protection assay where pregnant mice are passively immunized by injecting rabbit immune sera (or control sera) approximately 2 days before delivery. The pups are then challenged with a lethal dose of GBS.

Specifically, the Passive Maternal Immunization Assay referred to herein used groups of pregnant CD1 mice which were passively immunized by injecting 1 ml of rabbit immune sera or control sera via I.P., 2 days before delivery. Newborn mice (24-48 hrs after birth) are challenged via I.P. with a 70 - 90% lethal dose of GBS serotype III COH1. The challenge dose, obtained by diluting a frozen mid log phase culture, was administered in 50µl of THB medium.

For both assays, the number of pups surviving GBS infection was assessed every 12 hrs for 4 days. Statistical significance was estimated by Fisher's exact test.

The results of each assay for immunization with SEQ ID NO: 7, SEQ ID NO: 8, PBS and GBS whole cell are set forth in Tables 1 and 2 below.

TABLE 1: Active Maternal Immunization

Antigen	Alive/total	%Survival	Fisher's exact test
PBS (neg control)	13/80	16%	
GBS (whole cell)	54/65	83%	P<0.00000001
GBS80 (intact)	62/70	88%	P<0.00000001
GBS80 (fragment) SEQ ID 7	35/64	55%	P=0.0000013
GBS80 (fragment) SEQ ID 8	13/67	19%	P=0.66

Table 2: Passive Maternal Immunization

Antigen	Alive/total	%Survival	Fisher's exact test
PBS (neg control)	12/42	28%	
GBS (whole cell)	48/52	92%	P<0.00000001
GBS80 (intact)	48/55	87%	P<0.00000001
GBS80 (fragment) SEQ ID 7	45/57	79%	P=0.0000006
GBS80 (fragment) SEQ ID 8	13/54	24%	P=1

As shown in Tables 1 and 2, immunization with the SEQ ID NO: 7 GBS 80 fragment provided a substantially improved survival rate for the challenged pups than the comparison SEQ ID NO: 8 GBS 80 fragment. These results indicate that the SEQ ID NO: 7 GBS 80 fragment may comprise an important immunogenic epitope of GBS 80.

Combinations including GBS 80

The invention includes combinations of two or more GBS antigens wherein the combination includes GBS 80 or a fragment thereof. Applicants have discovered that GBS 80 is particularly suitable for immunization in combination with other GBS antigens and that these antigen combinations provide for a synergistic effect.

Preferably, the combination of GBS antigens consists of three, four, five, six, seven, eight, nine, or ten GBS antigens. Still more preferably, the combination of GBS antigens consists of three, four, or five GBS antigens.

Preferably, the combinations of the invention provide for improved immunogenicity over the immunogenicity of the antigens when administered alone. Improved immunogenicity may be measured, for

example, by the Active Maternal Immunization Assay. As discussed above, this assay may be used to measure serum titers of the female mice during the immunization schedule as well as the survival time of the pups after challenge. Preferably, immunization with the immunogenic compositions of the invention yield an increase of at least 2 percentage points (preferably at least 3, 4 or 5 percentage points) in the percent survival of the challenged pups as compared to the percent survival from maternal immunization with a single antigen of the composition when administered alone. Preferably, the increase is at least 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29 or 30 percentage points. Preferably, the GBS combinations of the invention comprising GBS 80 demonstrate an increase in the percent survival as compared to the percent survival from immunization with a non-GBS 80 antigen alone.

Examples of combinations of the invention which demonstrate improved immunogenicity are set forth below. A more detailed description of the GBS antigens referred to in these experiments is set forth following the examples.

EXAMPLE 1: Active Maternal Immunization Assay of GBS 80 alone vs. in combination

In this example, the Active Maternal Immunization Assay was used to measure the percent survival of pups challenged with a Type III serotype of GBS (COH1 isolate), at t=56 days. The maternal mice were immunized according to the Active Maternal Immunization Assay schedule discussed above with GBS 80 alone, combinations of GBS antigens (with and without GBS 80), placebo (PBS) or inactivated whole cell GBS isolate as indicated in Table 3 below. In these experiments, the challenge dose for GBS Type III, strain isolate COH1 sufficient to kill 70 – 90 % of unimmunized pups is approximately equal to 10 x LD 50% (where LD 50% is the statistically derived Median Lethal Dose).

Table 3: Active Maternal Immunization Assay of GBS 80 alone vs. in combination

	I Challenge t=56 days Type III COH1 10 x LD 50%	
α-GBS	Alive/treated	Survival %
α-PBS	3/26	11
α-GBS III	9/20	45
80	24/34	70
80+338+330	39/40	97
80+330+104	38/40	95
80+104+404	24/24	100
80+338+104	33/34	97
80+338+404	30/30	100
338+330+104	22/30	73
338+104+404	24/37	65
80+330+404	25/28	89

As shown in Table 3, combinations of GBS antigens which included GBS 80 demonstrated an improved immunogenicity over the use of the antigens alone. For example, immunization with GBS 80 alone yielded a 70% survival rate among the challenged pups. Immunization with combinations of GBS 80 with GBS 338, GBS 330, GBS 104, and GBS 404 yielded 95 to 100% survival rate among the challenged pups. This is an increase of 25 to 30 percentage points.

By comparison, combinations of these antigens which did not include GBS 80 failed to achieve the % survival of GBS 80 alone. For example, immunization with GBS 338, GBS 104 and GBS 404 yielded a 65% survival rate. Replacement of any one of these antigens with GBS 80 dramatically increased the percent survival rate to between 97 and 100%. This is an increase of 32 to 35 percentage points. (See percent survival rates of GBS 80, 338, 101 (97%); GBS 80, 338, 404 (100%) and GBS 80, 104, 404 (100%)). Similarly, immunization with GBS 338, 330 and 104 yielded a 73% survival rate. Replacement of any one of these antigens with GBS 80 increased the percent survival rate to between 95 – 97%.

EXAMPLE 2: Active Maternal Immunization Assay of GBS 80, GBS 322, GBS 276, GBS 104 alone vs. in combination

In this example, the Active Maternal Immunization Assay was used to measure the percent survival of pups challenged with a Type III serotype of GBS (COH1 isolate) at t=56 days. The maternal mice were immunized according to the Active Maternal Immunization Assay schedule discussed above with a single GBS antigen, combinations of GBS antigens with GBS 80, and placebo (PBS) as indicated in Table 4 below.

Table 4: Active Maternal Immunization Assay of GBS 80, GBS 322, GBS 276 or GBS 104 alone vs. in combination with GBS 80

	I Challenge t=56 days Type III COH1 10x LD 50%	
α-GBS	**Alive/treated**	**Survival %**
80 + 322 + 104	**27/27**	**100**
80 + 322 + 276	**35/38**	**92**
80 + 322 + 91	**24/24**	**100**
80 + 104 + 276	**29/30**	**97**
80 + 104 + 91	**36/40**	**90**
80 + 276 + 91	**33/40**	**82**
GBS 80	**24/30**	**80**
GBS 322	**7/40**	**17**
GBS 276	**13/37**	**35**
GBS 104	**28/38**	**74**
α-PBS	**2/27**	**7**

As shown in Table 4, the combinations of the antigens with GBS 80 yielded improved immunogenicity over the use of the antigens alone. For example, immunization with GBS 322 alone yielded a 17 % survival rate among the challenged pups. Immunization with combinations of GBS 322 with GBS 80 and another GBS antigen yielded survival rates of 92 – 100%. As another example, immunization with GBS 104 alone yielded a 74% survival rate. Immunization with combinations of GBS 104 with GBS 80 and another GBS antigen yielded survival rates of 90 – 100%. As another example, immunization with GBS 276 alone yielded a 35% survival rate. Immunization with combinations of GBS 276 with GBS 80 and another GBS antigen yielded survival rates of 82 – 97%.

Having demonstrated the immunogenicity of the above-described combinations, the duration of the immune response in the mouse model was further analysed. The maternal mice used in the above described Active Maternal Immunization Assay were mated a second time and the resulting pups challenged with a

different GBS serotype (Type V, CJB 111 isolate) at a dramatically higher dose (300x LD 50%) at t=91 days. The parameters of this second, much stronger challenge were outside those of the standard Active Maternal Immunization Assay and were meant to probe the limits of the immunological memory generated from the original maternal immunization in the mouse model. Indication of immunological memory in this model under these conditions is thought to be significant. As shown in Table 5, even under these extreme conditions, increased survival rates were generally achieved, particularly for the combination comprising GBS 80, GBS 322 and GBS 104. It was surprising to note that the percent survival rate for the combination of GBS 80, GBS 233 and GBS 104 was 100% for both the first and second challenges.

Table 5: Second generation pups challenged with higher dose of different strain

α-GBS	II Challenge t=91 days Type V CJB111 300x LD 50% Alive/treated	Survival %
80 + 322 + 104	**20/20**	**100**
80 + 322 + 276	**32/37**	**86**
80 + 322 + 91	**27/30**	**90**
80 + 104 + 276	**22/37**	**59**
80 + 104 + 91	**36/39**	**92**
80 + 276 + 91	**23/28**	**82**
GBS 80	**13/30**	**43**
GBS 322	**25/30**	**83**
GBS 276	**18/40**	**45**
GBS 104	**21/39**	**54**
α-PBS	**9/36**	**25**

EXAMPLE 3: Active Maternal Immunization Assay of combinations of GBS 80 with GBS 690, GBS 691, GBS 338, GBS 305, GBS 361 and GBS 184

In this example additional combinations of GBS antigens were used in the Active Maternal Immunization Assay, again with a GBS Type III COH1 isolate challenge. The maternal mice were immunized according to the Active Maternal Immunization Assay schedule described above with the combinations of GBS antigens set forth in Table 6 below.

Table 6: Active Maternal Immunization Assay using combinations of GBS 80 with GBS 690, GBS 691, GBS 338, GBS 305, GBS 361 and GBS 184

	I Challenge t=56 days Type III COH1 10x LD 50%	
α-GBS	Alive/treated	Survival %
80 + 690 + 691	**26/29**	**90**
80 + 690 + 338	**35/40**	**87**
80 + 690 + 305	**34/35**	**97**
80 + 691 + 305	**37/40**	**92**
80 + 338 + 305	***25/30***	***83***
80 + 338 + 361	**26/30**	**87**
80 + 305 +361	**23/30**	**77**
80 + 184 + 691	**32/39**	**82**
α-PBS	**10/40**	**25**

The maternal mice in this model were also mated a second time and the resulting pups challenged with a the same GBS isolate at a dramatically higher dose (100x LD 50%) at t=84 days. As in the example above, the parameters of this second, much stronger challenge were outside those of the standard Active Maternal Immunization Assay and were meant to probe the limits of the immunological memory generated from the original maternal immunization in the mouse model. As shown in Table 7, even under these extreme conditions, some of the survival rates remained at or above 70%. Surprisingly, the percent survival rates for the combination of GBS 80, GBS 184 and GBS 691 actually increased.

Table 7: Second generation pups challenged with higher dose

	II Challenge t=84 days Type III COH1 100x LD 50%	
α-GBS	Alive/treated	Survival %
80 + 690 + 691	**19/39**	**49**
80 + 690 + 338	**21/30**	**70**
80 + 690 + 305	**23/40**	**57**
80 + 691 + 305	**22/30**	**73**
80 + 338 + 305	**18/30**	**60**
80 + 338 + 361	**25/40**	**62**
80 + 305 +361	**21/30**	**70**
80 + 184 + 691	**35/40**	**87**
α-PBS	**4/20**	**20**

EXAMPLE 4: Active Maternal Immunization Assay using combinations of GBS 80 with GBS 690, GBS 691, GBS 338, GBS 305, and GBS 361

In this example additional combinations of GBS antigens were used in the Active Maternal Immunization Assay, this time with a GBS Type V, CJB111 isolate challenge. In these experiments, the challenge dose for the GBS Type V, CJB111 isolate sufficient to kill 70 – 90% of unimmunized pups is approximately equal to 60 x LD 50% (where LD 50% is the statistically derived Median Lethal Dose). The maternal mice were immunized according to the Active Maternal Immunization Assay schedule described

above with the combinations of GBS antigens set forth in Table 8 below. As shown in Table 8, in this particular challenge study with this specific Type V strain isolate, the survival rates for all of the combinations achieved at least 70%.

Table 8: Active Maternal Immunization Assay using combinations of GBS 80 with GBS 690, GBS 691, GBS 338, GBS 305 and GBS 361

	I Challenge t=56 days Type V CJB111 60x LD 50%	
α-GBS	Alive/treated	Survival %
80 + 690 + 691	24/30	80
80 + 690 + 338	11/17	70
80 + 691 + 338	7/10	70
80 + 691 + 305	21/30	70
80 + 338 + 305	26/30	87
80 + 338 + 361	26/30	87
80 + 305 +361	28/30	93
GBS 80	21/30	70
α-PBS	5/18	28

The maternal mice in this model were also mated a second time and the resulting pups challenged with a the same GBS isolate at a dramatically higher dose (600x LD 50%) at t=84 days. As in the example above, the parameters of this second, much stronger challenge were outside those of the standard Active Maternal Immunization Assay and were meant to probe the limits of the immunological memory generated from the original maternal immunization in the mouse model. As shown in Table 9, even under these extreme conditions, some of the survival rates remained above 70%. Surprisingly, the percent survival for two of the antigen groups actually increased (GBS 80, GBS 690 and GBs 338) and (GBS 80, GBS 691 and GBS 338).

Table 9: Second generation pups challenged with higher dose

	II Challenge t=84 days Type V CJB111 600x LD 50%	
α-GBS	Alive/treated	Survival %
80 + 690 + 691	27/37	73
80 + 690 + 338	15/20	75
80 + 691 + 338	27/30	90
80 + 691 + 305	23/40	57
80 + 338 + 305	12/20	60
80 + 338 + 361	24/30	80
80 + 305 +361	24/30	80
GBS 80	24/30	80
α-PBS	ND	ND

Accordingly, the invention therefore includes compositions comprising combinations of two or more GBS antigens, wherein the combination includes GBS 80 or a fragment thereof or a polypeptide sequence having sequence identity thereto.

In one embodiment, the combination may consist of two to thirteen GBS antigens selected from the group consisting of GBS 80, GBS 91, GBS 104, GBS 184, GBS 276, GBS 305, GBS 322, GBS 330, GBS 338, GBS 361, GBS 404, GBS 690, and GBS 691. Preferably, the combination includes GBS 80 in combination with one or more of GBS 104 and GBS 322.

Instead of the full length antigen, the combination may comprise an immunogenic fragment of the selected GBS antigen and/or a polypeptide sequence having sequence identity to the selected antigen.

Preferably, the combination of GBS antigens consists of three, four, five, six, seven, eight, nine, or ten GBS antigens. Still more preferably, the combination of GBS antigens consists of three, four, or five GBS antigens.

Details of examples of GBS antigens for use in combination with GBS 80 are set forth below.

GBS 91

GBS 91 refers to a GBS C3 binding polypeptide. Nucleotide and amino acid sequences of GBS 91 sequenced from serotype V isolated strain 2603 V/R are set forth in Ref. 3 as SEQ ID 8937 and SEQ ID 8938. These sequences are set forth below as SEQ ID NOS 10 and 11:

SEQ ID NO. 10

ATGAAAAAGGACAAGTAAATGATACTAAGCAATCTTACTCTCTACGTAAATATAAATTTGGTTTAGCATCA
GTAATTTTAGGGTCATTCATAATGGTCACAAGTCCTGTTTTTGCGGATCAAACTACATCGGTTCAAGTTAAT
AATCAGACAGGCACTAGTGTGGATGCTAATAATTCTTCCAATGAGACAAGTGCGTCAAGTGTGATTACTTCC
AATAATGATAGTGTTCAAGCGTCTGATAAAGTTGTAAATAGTCAAAATACGGCAACAAAGGACATTACTACT
CCTTTAGTAGAGACAAAGCCAATGGTGGAAAAAACATTACCTGAACAAGGGAATTATGTTTATAGCAAAGAA
ACCGAGGTGAAAAATACACCTTCAAAATCAGCCCCAGTAGCTTTCTATGCAAAGAAAGGTGATAAAGTTTTC
TATGACCAAGTATTTAATAAAGATAATGTGAAATGGATTTCATATAAGTCTTTTTGTGGCGTACGTCGATAC
GCAGCTATTGAGTCACTAGATCCATCAGGAGGTTCAGAGACTAAAGCACCTACTCCTGTAACAAATTCAGGA
AGCAATAATCAAGAGAAAATAGCAACGCAAGGAAATTATACATTTTCACATAAAGTAGAAGTAAAAAATGAA
GCTAAGGTAGCGAGTCCAACTCAATTTACATTGGACAAAGGAGACAGAATTTTTTACGACCAAATACTAACT
ATTGAAGGAAATCAGTGGTTATCTTATAAATCATTCAATGGTGTTCGTCGTTTTGTTTTGCTAGGTAAAGCA
TCTTCAGTAGAAAAAACTGAAGATAAAGAAAAAGTGTCTCCTCAACCACAAGCCCGTATTACTAAAACTGGT
AGACTGACTATTTCTAACGAAACAACTACAGGTTTTGATATTTTAATTACGAATATTAAAGATGATAACGGT
ATCGCTGCTGTTAAGGTACCGGTTTGGACTGAACAAGGAGGCAAGATGATATTAAATGGTATACAGCTGTA
ACTACTGGGGATGGCAACTACAAAGTAGCTGTATCATTTGCTGACCATAAGAATGAGAAGGGTCTTTATAAT
ATTCATTTATACTACCAAGAAGCTAGTGGGACACTTGTAGGTGTAACAGGAACTAAAGTGACAGTAGCTGGA
ACTAATTCTTCTCAAGAACCTATTGAAAATGGTTTAGCAAAGACTGGTGTTTATAATATTATCGGAAGTACT
GAAGTAAAAAATGAAGCTAAAATATCAAGTCAGACCCAATTTACTTTAGAAAAAGGTGACAAAATAAATTAT
GATCAAGTATTGACAGCAGATGGTTACCAGTGGATTTCTTACAAATCTTATAGTGGTGTTCGTCGCTATATT
CCTGTGAAAAAGCTAACTACAAGTAGTGAAAAAGCGAAAGATGAGGCGACTAAACCGACTAGTTATCCCAAC
TTACCTAAAACAGGTACCTATACATTTACTAAAACTGTAGATGTGAAAAGTCAACCTAAAGTATCAAGTCCA
GTGGAATTTAATTTTCAAAAGGGTGAAAAAATACATTATGATCAAGTGTTAGTAGTAGATGGTCATCAGTGG
ATTTCATACAAGAGTTATTCCGGTATTCGTCGCTATATTGAAATT

SEQ ID NO. 11

MKKGQVNDTKQSYSLRKYKFGLASVILGSFIMVTSPVFADQTTSVQVNNQTGTSVDANNSSNETSASSVITS
NNDSVQASDKVVNSQNTATKDITTPLVETKPMVEKTLPEQGNYVYSKETEVKNTPSKSAPVAFYAKKGDKVF
YDQVFNKDNVKWISYKSFCGVRRYAAIESLDPSGGSETKAPTPVTNSGSNNQEKIATQGNYTFSHKVEVKNE
AKVASPTQFTLDKGDRIFYDQILTIEGNQWLSYKSFNGVRRFVLLGKASSVEKTEDKEKVSPQPQARITKTG

RLTISNETTTGFDILITNIKDDNGIAAVKVPVWTEQGGQDDIKWYTAVTTGDGNYKVAVSFADHKNEKGLYN
IHLYYQEASGTLVGVTGTKVTVAGTNSSQEPIENGLAKTGVYNIIGSTEVKNEAKISSQTQFTLEKGDKINY
DQVLTADGYQWISYKSYSGVRRYIPVKKLTTSSEKAKDEATKPTSYPNLPKTGTYTFTKTVDVKSQPKVSSP
VEFNFQKGEKIHYDQVLVVDGHQWISYKSYSGIRRYIEI

5

GBS 91 contains an N-terminal leader or signal sequence region which is indicated by the underlined sequence at the beginning of SEQ ID NO: 11 above. In one embodiment, one or more amino acids from this leader or signal sequence region of GBS 91 are removed. An example of such a GBS 91 fragment is set forth below as SEQ ID NO: 12.

10 **SEQ ID NO: 12**
DQTTSVQVNNQTGTSVDANNSSNETSASSVITSNNDSVQASDKVVNSQNTATKDITTPLVETKPMVEKTLPE
QGNYVVSKETEVKNTPSKSAPVAFYAKKGDKVFYDQVFNKDNVKWISYKSFCGVRRYAAIESLDPSGGSETK
APTPVTNSGSNNQEKIATQGNYTFSHKVEVKNEAKVASPTQFTLDKGDRIFYDQILTIEGNQWLSYKSFNGV
RRFVLLGKASSVEKTEDKEKVSPQPQARITKTGRLTISNETTTGFDILITNIKDDNGIAAVKVPVWTEQGGQ
15 DDIKWYTAVTTGDGNYKVAVSFADHKNEKGLYNIHLYYQEASGTLVGVTGTKVTVAGTNSSQEPIENGLAKT
GVYNIIGSTEVKNEAKISSQTQFTLEKGDKINYDQVLTADGYQWISYKSYSGVRRYIPVKKLTTSSEKAKDE
ATKPTSYPNLPKTGTYTFTKTVDVKSQPKVSSPVEFNFQKGEKIHYDQVLVVDGHQWISYKSYSGIRRYIEI

GBS 91 contains a C-terminal transmembrane region which may be located within the underlined

20 region near the end of SEQ ID NO: 11 above. In one embodiment, one or more amino acids from the transmembrane and cytoplasmic regions are removed. An example of such a GBS 91 fragment is set forth below as SEQ ID NO: 13.

SEQ ID NO: 13
MKKGQVNDTKQSYSLRKYKFGLASVILGSFIMVTSPVFADQTTSVQVNNQTGTSVDANNSSNETSASSVITS
25 NNDSVQASDKVVNSQNTATKDITTPLVETKPMVEKTLPEQGNYVVSKETEVKNTPSKSAPVAFYAKKGDKVF
YDQVFNKDNVKWISYKSFCGVRRYAAIESLDPSGGSETKAPTPVTNSGSNNQEKIATQGNYTFSHKVEVKNE
AKVASPTQFTLDKGDRIFYDQILTIEGNQWLSYKSFNGVRRFVLLGKASSVEKTEDKEKVSPQPQARITKTG
RLTISNETTTGFDILITNIKDDNGIAAVKVPVWTEQGGQDDIKWYTAVTTGDGNYKVAVSFADHKNEKGLYN
IHLYYQEASGTLVGVTGTKVTVAGTNSSQEPIENGLAKTGVYNIIGSTEVKNEAKISSQTQFTLEKGDKINY
30 DQVLTADGYQWISYKSYSGVRRYIPVKKLTTSSEKAKDEATKPTSYPNLPKTG

GBS 91 contains an amino acid motif indicative of a cell wall anchor: **SEQ ID NO: 14** LTKTG (shown in italics in SEQ ID NO: 11 above). In one embodiment, both the transmembrane domain and the cell wall anchor motif are removed from GBS 91. An example of such a GBS 91 fragment is set forth below

35 as SEQ ID NO: 14.

SEQ ID NO: 14
MKKGQVNDTKQSYSLRKYKFGLASVILGSFIMVTSPVFADQTTSVQVNNQTGTSVDANNSSNETSASSVITS
NNDSVQASDKVVNSQNTATKDITTPLVETKPMVEKTLPEQGNYVVSKETEVKNTPSKSAPVAFYAKKGDKVF
YDQVFNKDNVKWISYKSFCGVRRYAAIESLDPSGGSETKAPTPVTNSGSNNQEKIATQGNYTFSHKVEVKNE
40 AKVASPTQFTLDKGDRIFYDQILTIEGNQWLSYKSFNGVRRFVLLGKASSVEKTEDKEKVSPQPQARITKTG
RLTISNETTTGFDILITNIKDDNGIAAVKVPVWTEQGGQDDIKWYTAVTTGDGNYKVAVSFADHKNEKGLYN
IHLYYQEASGTLVGVTGTKVTVAGTNSSQEPIENGLAKTGVYNIIGSTEVKNEAKISSQTQFTLEKGDKINY
DQVLTADGYQWISYKSYSGVRRYIPVKKLTTSSEKAKDEATKPTSYPN

45 In one embodiment, one or more amino acids from the leader or signal sequence region and one or more amino acids from the transmembrane and cytoplasmic regions are removed from the GBS 91 sequence. An example of such a GBS 91 fragment is set forth below as SEQ ID NO: 15.

SEQ ID NO: 15
DQTTSVQVNNQTGTSVDANNSSNETSASSVITSNNDSVQASDKVVNSQNTATKDITTPLVETKPMVEKTLPE
QGNYVYSKETEVKNTPSKSAPVAFYAKKGDKVFYDQVFNKDNVKWISYKSFCGVRRYAAIESLDPSGGSETK
APTPVTNSGSNNQEKIATQGNYTFSHKVEVKNEAKVASPTQFTLDKGDRIFYDQILTIEGNQWLSYKSFNGV
RRFVLLGKASSVEKTEDKEKVSPQPQARITKTGRLTISNETTTGFDILITNIKDDNGIAAVKVPVWTEQGGQ
DDIKWYTAVTTGDGNYKVAVSFADHKNEKGLYNIHLYYQEASGTLVGVTGTKVTVAGTNSSQEPIENGLAKT
GVYNIIGSTEVKNEAKISSQTQFTLEKGDKINYDQVLTADGYQWISYKSYSGVRRYIPVKKLTTSSEKAKDE
ATKPTSYPNLPKTG

In another embodiment, the leader or signal sequence region, the transmembrane and cytoplasmic regions, and the cell wall anchor motif are all removed from the GBS 91 sequence. An example of such a GBS 91 fragment is set forth below as SEQ ID NO: 16.

SEQ ID NO: 16
DQTTSVQVNNQTGTSVDANNSSNETSASSVITSNNDSVQASDKVVNSQNTATKDITTPLVETKPMVEKTLPE
QGNYVYSKETEVKNTPSKSAPVAFYAKKGDKVFYDQVFNKDNVKWISYKSFCGVRRYAAIESLDPSGGSETK
APTPVTNSGSNNQEKIATQGNYTFSHKVEVKNEAKVASPTQFTLDKGDRIFYDQILTIEGNQWLSYKSFNGV
RRFVLLGKASSVEKTEDKEKVSPQPQARITKTGRLTISNETTTGFDILITNIKDDNGIAAVKVPVWTEQGGQ
DDIKWYTAVTTGDGNYKVAVSFADHKNEKGLYNIHLYYQEASGTLVGVTGTKVTVAGTNSSQEPIENGLAKT
GVYNIIGSTEVKNEAKISSQTQFTLEKGDKINYDQVLTADGYQWISYKSYSGVRRYIPVKKLTTSSEKAKDE
ATKPTSYPN

Further information regarding GBS 91 can be found in WO 01/25440 (C3 binding polypeptide), WO 01/32882 (ID-65), WO 02/31156 (BVH) and Reinscheid et al., *Microbiology* (2002) 148: 3245-3254 (*bsp* gene), each of which are incorporated herein by reference in their entirety.

GBS 104

GBS 104 refers to a putative cell wall surface anchor family protein. It has been referred to as emaA protein. Nucleotide and amino acid sequences of GBS 104 sequenced from serotype V isolated strain 2603 V/R are set forth in Ref. 3 as SEQ ID 8777 and SEQ ID 8778. These sequences are set forth below as SEQ ID NOS 17 and 18:

SEQ ID NO. 17
ATGAAAAAGAGACAAAAAATATGGAGAGGGTTATCAGTTACTTTACTAATCCTGTCCCAAATTCCATTTGGT
ATATTGGTACAAGGTGAAACCCAAGATACCAATCAAGCACTTGGAAAAGTAATTGTTAAAAAAACGGGAGAC
AATGCTACACCATTAGGCAAAGCGACTTTTGTGTTAAAAAATGACAATGATAAGTCAGAAACAAGTCACGAA
ACGGTAGAGGGTTCTGGAGAAGCAACCTTTGAAAACATAAAACCTGGAGACTACACATTAAGAGAAGAAACA
GCACCAATTGGTTATAAAAAAACTGATAAAACCTGGAAAGTTAAAGTTGCAGATAACGGAGCAACAATAATC
GAGGGTATGGATGCAGATAAAGCAGAGAAACGAAAAGAAGTTTTGAATGCCCAATATCCAAAATCAGCTATT
TATGAGGATACAAAAGAAAATTACCCATTAGTTAATGTAGAGGGTTCCAAAGTTGGTGAACAATACAAAGCA
TTGAATCCAATAAATGGAAAAGATGGTCGAAGAGAGATTGCTGAAGGTTGGTTATCAAAAAAAATTACAGGG
GTCAATGATCTCGATAAGAATAAATATAAAATTGAATTAACTGTTGAGGGTAAAACCACTGTTGAAACGAAA
GAACTTAATCAACCACTAGATGTCGTTGTGCTATTAGATAATTCAAATAGTATGAATAATGAAAGAGCCAAT
AATTCTCAAAGAGCATTAAAAGCTGGGGAAGCAGTTGAAAAGCTGATTGATAAAATTACATCAAATAAAGAC
AATAGAGTAGCTCTTGTGACATATGCCTCAACCATTTTGATGGTACTGAAGCGACCGTATCAAAGGAGTT
GCCGATCAAAATGGTAAAGCGCTGAATGATAGTGTATCATGGGATTATCATAAAACTACTTTTACAGCAACT
ACACATAATTACAGTTATTTAAATTTAACAAATGATGCTAACGAAGTTAATATTCTAAAGTCAAGAATTCCA
AAGGAAGCGGAGCATATAAATGGGGATCGCACGCTCTATCAATTTGGTGCGACATTTACTCAAAAAGCTCTA
ATGAAAGCAAATGAAATTTTAGAGACACAAAGTTCTAATGCTAGAAAAAAACTTATTTTTCACGTAACTGAT
GGTGTCCCTACGATGTCTTATGCCATAAATTTTAATCCTTATATATCAACATCTTACCAAAACCAGTTTAAT
TCTTTTTTAAATAAAATACCAGATAGAAGTGGTATTCTCCAAGAGGATTTTATAATCAATGGTGATGATTAT
CAAATAGTAAAAGGAGATGGAGAGAGTTTTAAACTGTTTTCGGATAGAAAAGTTCCTGTTACTGGAGGAACG

ACACAAGCAGCTTATCGAGTACCGCAAAATCAACTCTCTGTAATGAGTAATGAGGGATATGCAATTAATAGT
GGATATATTTATCTCTATTGGAGAGATTACAACTGGGTCTATCCATTTGATCCTAAGACAAAGAAAGTTTCT
GCAACGAAACAAATCAAAACTCATGGTGAGCCAACAACATTATACTTTAATGGAAATATAAGACCTAAAGGT
TATGACATTTTTACTGTTGGGATTGGTGTAAACGGAGATCCTGGTGCAACTCCTCTTGAAGCTGAGAAATTT
ATGCAATCAATATCAAGTAAAACAGAAAATTATACTAATGTTGATGATACAAATAAAATTTATGATGAGCTA
AATAAATACTTTAAAACAATTGTTGAGGAAAAACATTCTATTGTTGATGGAAATGTGACTGATCCTATGGGA
GAGATGATTGAATTCCAATTAAAAAATGGTCAAAGTTTTACACATGATGATTACGTTTTGGTTGGAAATGAT
GGCAGTCAATTAAAAAATGGTGTGGCTCTTGGTGGACCAAACAGTGATGGGGGAATTTTAAAAGATGTTACA
GTGACTTATGATAAGACATCTCAAACCATCAAAATCAATCATTTGAACTTAGGAAGTGGACAAAAAGTAGTT
CTTACCTATGATGTACGTTTAAAAGATAACTATATAAGTAACAAATTTTACAATACAAATAATCGTACAACG
CTAAGTCCGAAGAGTGAAAAAGAACCAAATACTATTCGTGATTTCCCAATTCCCAAAATTCGTGATGTTCGT
GAGTTTCCGGTACTAACCATCAGTAATCAGAAGAAAATGGGTGAGGTTGAATTTATTAAAGTTAATAAAGAC
AAACATTCAGAATCGCTTTTGGGAGCTAAGTTTCAACTTCAGATAGAAAAAGATTTTTCTGGGTATAAGCAA
TTTGTTCCAGAGGGAAGTGATGTTACAACAAAGAATGATGGTAAAATTTATTTTAAAGCACTTCAAGATGGT
AACTATAAATTATATGAAATTTCAAGTCCAGATGGCTATATAGAGGTTAAAACGAAACCTGTTGTGACATTT
ACAATTCAAAATGGAGAAGTTACGAACCTGAAAGCAGATCCAAATGCTAATAAAAATCAAATCGGGTATCTT
GAAGGAAATGGTAAACATCTTATTACCAACACTCCCAAACGCCCACCAGGTGTTTTCCTAAAACAGGGGGA
ATTGGTACAATTGTCTATATATTAGTTGGTTCTACTTTTATGATACTTACCATTTGTTCTTCCGTCGTAAA
CAATTG

SEQ ID NO. 18

MKKRQKIWRGLSVTLLILSQIPPGILVQGETQDTNQALGKVIVKKTGDNATPLGKATFVLKNDNDKSETSHE
TVEGSGEATFENIKPGDYTLREETAPIGYKKTDKTWKVKVADNGATIIEGMDADKAEKRKEVLNAQYPKSAI
YEDTKENYPLVNVEGSKVGEQYKALNPINGKDGRREIAEGWLSKKITGVNDLDKNKYKIELTVEGKTTVETK
ELNQPLDVVVLLDNSNSMNNERANNSQRALKAGEAVEKLIDKITSNKDNRVALVTYASTIFDGTEATVSKGV
ADQNGKALNDSVSWDYHKTTFTATTHNYSYLNLTNDANEVNILKSRIPKEAEHINGDRTLYQFGATFTQKAL
MKANEILETQSSNARKKLIFHVTDGVPTMSYAINFNPYISTSYQNQFNSFLNKIPDRSGILQEDFIINGDDY
QIVKGDGESFKLFSDRKVPVTGGTTQAAYRVPQNQLSVMSNEGYAINSGYIYLYWRDYNWVYPFDPKTKKVS
ATKQIKTHGEPTTLYFNGNIRPKGYDIFTVGIGVNGDPGATPLEAEKFMQSISSKTENYTNVDDTNKIYDEL
NKYFKTIVEEKHSIVDGNVTDPMGEMIEFQLKNGQSFTHDDYVLVGNDGSQLKNGVALGGPNSDGGILKDVT
VTYDKTSQTIKINHLNLGSGQKVVLTYDVRLKDNYISNKFYNTNNRTTLSPKSEKEPNTIRDFPIPKIRDVR
EFPVLTISNQKKMGEVEFIKVNKDKHSESLLGAKFQLQIEKDFSGYKQFVPEGSDVTTKNDGKIYFKALQDG
NYKLYEISSPDGYIEVKTKPVVTFTIQNGEVTNLKADPNANKNQIGYLEGNGKHLITNTPKRPPGVFPKTGG
IGTIVYILVGSTFMILTICSFRRKQL

GBS 104 contains an N-terminal leader or signal sequence region which is indicated by the underlined sequence at the beginning of SEQ ID NO 18 above. In one embodiment, one or more amino acid sequences from the leader or signal sequence region of GBS 104 are removed. An example of such a GBS 104 fragment is set forth below as SEQ ID NO 19.

SEQ ID NO 19

GETQDTNQALGKVIVKKTGDNATPLGKATFVLKNDNDKSETSHETVEGSGEATFENIKPGDYTLREETAPIG
YKKTDKTWKVKVADNGATIIEGMDADKAEKRKEVLNAQYPKSAIYEDTKENYPLVNVEGSKVGEQYKALNPI
NGKDGRREIAEGWLSKKITGVNDLDKNKYKIELTVEGKTTVETKELNQPLDVVVLLDNSNSMNNERANNSQR
ALKAGEAVEKLIDKITSNKDNRVALVTYASTIFDGTEATVSKGVADQNGKALNDSVSWDYHKTTFTATTHNY
SYLNLTNDANEVNILKSRIPKEAEHINGDRTLYQFGATFTQKALMKANEILETQSSNARKKLIFHVTDGVPT
MSYAINFNPYISTSYQNQFNSFLNKIPDRSGILQEDFIINGDDYQIVKGDGESFKLFSDRKVPVTGGTTQAA
YRVPQNQLSVMSNEGYAINSGYIYLYWRDYNWVYPFDPKTKKVSATKQIKTHGEPTTLYFNGNIRPKGYDIF
TVGIGVNGDPGATPLEAEKFMQSISSKTENYTNVDDTNKIYDELNKYFKTIVEEKHSIVDGNVTDPMGEMIE
FQLKNGQSFTHDDYVLVGNDGSQLKNGVALGGPNSDGGILKDVTVTYDKTSQTIKINHLNLGSGQKVVLTYD
VRLKDNYISNKFYNTNNRTTLSPKSEKEPNTIRDFPIPKIRDVREFPVLTISNQKKMGEVEFIKVNKDKHSE
SLLGAKFQLQIEKDFSGYKQFVPEGSDVTTKNDGKIYFKALQDGNYKLYEISSPDGYIEVKTKPVVTFTIQN
GEVTNLKADPNANKNQIGYLEGNGKHLITNTPKRPPGVFPKTGGIGTIVYILVGSTFMILTICSFRRKQL

GBS 104 contains a C-terminal transmembrane and/or cytoplasmic region which is indicated by the underlined region near the end of SEQ ID NO 18 above. In one embodiment, one or more amino acids from the transmembrane or cytomplasmic regions are removed. An example of such a GBS 104 fragment is set forth below as SEQ ID NO 20.

SEQ ID NO: 20

MKKRQKIWRGLSVTLLILSQIPFGILVQGETQDTNQALGKVIVKKTGDNATPLGKATFVLKNDNDKSETSHE
TVEGSGEATFENIKPGDYTLREETAPIGYKKTDKTWKVKVADNGATIIEGMDADKAEKRKEVLNAQYPKSAI
YEDTKENYPLVNVEGSKVGEQYKALNPINGKDGRREIAEGWLSKKITGVNDLDKNKYKIELTVEGKTTVETK
ELNQPLDVVVLLDNSNSMNNERANNSQRALKAGEAVEKLIDKITSNKDNRVALVTYASTIFDGTEATVSKGV
ADQNGKALNDSVSWDYHKTTFTATTHNYSYLNLTNDANEVNILKSRIPKEAEHINGDRTLYQFGATFTQKAL
MKANEILETQSSNARKKLIFHVTDGVPTMSYAINFNPYISTSYQNQFNSFLNKIPDRSGILQEDFIINGDDY
QIVKGDGESFKLFSDRKVPVTGGTTQAAYRVPQNQLSVMSNEGYAINSGYIYLYWRDYNWVYPFDPKTKKVS
ATKQIKTHGEPTTLYFNGNIRPKGYDIFTVGIGVNGDPGATPLEAEKFMQSISSKTENYTNVDDTNKIYDEL
NKYFKTIVEEKHSIVDGNVTDPMGEMIEFQLKNGQSFTHDDYVLVGNDGSQLKNGVALGGPNSDGGILKDVT
VTYDKTSQTIKINHLNLGSGQKVVLTYDVRLKDNYISNKFYNTNNRTTLSPKSEKEPNTIRDFPIPKIRDVR
EFPVLTISNQKKMGEVEFIKVNKDKHSESLLGAKFQLQIEKDFSGYKQFVPEGSDVTTKNDGKIYFKALQDG
NYKLYEISSPDGYIEVKTKPVVTFTIQNGEVTNLKADPNANKNQIGYLEGNGKHLITNT

In one embodiment, one or more amino acids from the leader or signal sequence region and one or more amino acids from the transmembrane or cytoplasmic regions are removed. An example of such a GBS 104 fragment is set forth below as SEQ ID NO 21.

SEQ ID NO: 21

GETQDTNQALGKVIVKKTGDNATPLGKATFVLKNDNDKSETSHETVEGSGEATFENIKPGDYTLREETAPIG
YKKTDKTWKVKVADNGATIIEGMDADKAEKRKEVLNAQYPKSAIYEDTKENYPLVNVEGSKVGEQYKALNPI
NGKDGRREIAEGWLSKKITGVNDLDKNKYKIELTVEGKTTVETKELNQPLDVVVLLDNSNSMNNERANNSQR
ALKAGEAVEKLIDKITSNKDNRVALVTYASTIFDGTEATVSKGVADQNGKALNDSVSWDYHKTTFTATTHNY
SYLNLTNDANEVNILKSRIPKEAEHINGDRTLYQFGATFTQKALMKANEILETQSSNARKKLIFHVTDGVPT
MSYAINFNPYISTSYQNQFNSFLNKIPDRSGILQEDFIINGDDYQIVKGDGESFKLFSDRKVPVTGGTTQAA
YRVPQNQLSVMSNEGYAINSGYIYLYWRDYNWVYPFDPKTKKVSATKQIKTHGEPTTLYFNGNIRPKGYDIF
TVGIGVNGDPGATPLEAEKFMQSISSKTENYTNVDDTNKIYDELNKYFKTIVEEKHSIVDGNVTDPMGEMIE
FQLKNGQSFTHDDYVLVGNDGSQLKNGVALGGPNSDGGILKDVTVTYDKTSQTIKINHLNLGSGQKVVLTYD
VRLKDNYISNKFYNTNNRTTLSPKSEKEPNTIRDFPIPKIRDVREFPVLTISNQKKMGEVEFIKVNKDKHSE
SLLGAKFQLQIEKDFSGYKQFVPEGSDVTTKNDGKIYFKALQDGNYKLYEISSPDGYIEVKTKPVVTFTIQN
GEVTNLKADPNANKNQIGYLEGNGKHLITNT

GBS 184

GBS 184 refers to a putative lipoprotein. Nucleotide and amino acid sequences of GBS 184 sequenced from serotype V isolated strain 2603 V/R are set forth in Ref. 3 as SEQ ID 1977 and SEQ ID 1978. These sequences are also set forth below as SEQ ID NOS 22 and 23.

SEQ ID NO: 22

ATGAAAAAACAAAAACTATTACTGCTTATTGGAGGCTTATTAATAATGATAATGATGACAGCATGTAAGGAT
TCAAAAATCCCAGAAAACCGCACAAAGGAAGAGTACCAAGCTGAACAAAATTTTAAACCGTTTTTTGAGTTT
TTAGCACAAAAAGATAAAGATTTGAGCAAAATACAAAAATACTTACTATTAGTATCGGATTCAGGTGATGCA
TTAGATTTAGAATATTTCTATAGTATTCAAGATTTAAAAAAAATAAGGATTTAGGGAAGTTTGAAACAAGA
AAAAGTCAAATAGAAAAGCCGGGTGGCTATAATGAGTTAGAAAATAAAGAGGTCCCATTTGAATATTTTAAA
AATAATATAGTTTATCCAAAAGGAAAACCGAATATTACATTTGATGACTTTATTATCGGAGCAATGGATACT
AAAGAATTAAAAGAATTAAAAAAATTAAAAGTAAAAAGTTATTTATTAAAACATCCGGAAACTGAGTTGAAA
GATATAACATATGAATTGCCGACACAGTCGAAGCTTATTAAAAAA

SEQ ID NO: 23
MKKQKLLLLIGGLLIMIMMTACKDSKIPENRTKEEYQAEQNFKPFFEFLAQKDKDLSKIQKYLLLVSDSGDA
LDLEYFYSIQDLKKNKDLGKFETRKSQIEKPGGYNELENKEVPFEYFKNNIVYPKGKPNITFDDFIIGAMDT
KELKELKKLKVKSYLLKHPETELKDITYELPTQSKLIKK

GBS 184 contains a N-terminal leader or signal sequence region which is indicated by the underlined sequence at the beginning of SEQ ID NO 23, above. In one embodiment, one or more amino acids from the leader or signal sequence are removed from GBS 184. An example of such a GBS 184 fragment is set forth below as SEQ ID NO: 24.

SEQ ID NO: 24
KDSKIPENRTKEEYQAEQNFKPFFEFLAQKDKDLSKIQKYLLLVSDSGDALDLEYFYSIQDLKKNKDLGKFE
TRKSQIEKPGGYNELENKEVPFEYFKNNIVYPKGKPNITFDDFIIGAMDTKELKELKKLKVKSYLLKHPETE
LKDITYELPTQSKLIKK

GBS 276

GBS 276 refers to a C5a peptidase. Nucleotide and amino acid sequences of GBS 276 sequenced from serotype V isolated strain 2603 V/R are set forth in Ref. 3 as SEQ ID 8941 and SEQ ID 8942. These sequences are set forth below as SEQ ID NOS 25 and 26:

SEQ ID NO. 25
TTGCGTAAAAAACAAAAACTACCATTTGATAAACTTGCCATTGCGCTTATATCTACGAGCATCTTGCTCAAT
GCACAATCAGACATTAAAGCAAATACTGTGACAGAAGACACTCCTGCTACCGAACAAGCCGTAGAACCCCCA
CAACCAATAGCAGTTTCTGAGGAATCACGATCATCAAAGGAAACTAAAACCTCACAAACTCCTAGTGATGTA
GGAGAAACAGTAGCAGATGACGCTAATGATCTAGCCCCTCAAGCTCCTGCTAAAACTGCTGATACACCAGCA
ACCTCAAAAGCGACTATTAGGGATTTGAACGACCCTTCTCATGTCAAAACCCTGCAGGAAAAAGCAGGCAAG
GGAGCTGGGACCGTTGTTGCAGTGATTGATGCTGGTTTTGATAAAAATCATGAAGCGTGGCGCTTAACAGAC
AAAACTAAAGCACGTTACCAATCAAAAGAAAATCTTGAAAAAGCTAAAAAAGAGCACGGTATTACCTATGGC
GAGTGGGTCAATGATAAGGTTGCTTATTACCACGACTATAGTAAAGATGGTAAAAACGCTGTTGATCAAGAA
CACGGCACACACGTGTCAGGGATCTTGTCAGGAAATGCTCCATCTGAAATGAAAGAACCTTACCGCCTAGAA
GGTGCGATGCCTGAGGCTCAATTGCTTTTGATGCGTGTCGAAATTGTAAATGGACTAGCAGACTATGCTCGT
AACTACGCTCAAGCTATCAGAGATGCTGTCAACTTGGGAGCTAAGGTGATTAATATGAGCTTTGGTAATGCT
GCACTAGCTTACGCCAACCTTCCAGACGAAACCAAAAAAGCCTTTGACTATGCCAAATCAAAAGGTGTTAGC
ATTGTGACCTCAGCTGGTAATGATAGTAGCTTTGGGGGCAAGCCCCGTCTACCTCTAGCAGATCATCCTGAT
TATGGGGTGGTTGGGACACCTGCAGCGGCAGATTCAACATTGACAGTTGCTTCTTACAGCCCAGATAAACAG
CTCACTGAAACTGCTACGGTCAAAACAGACGATCATCAAGATAAAGAAATGCCTGTTATTTCAACAAACCGT
TTTGAGCCAAACAAGGCTTACGACTATGCTTATGCTAATCGTGGTACGAAAGAGGATGATTTTAAGGATGTC
GAAGGTAAGATTGCCCTTATTGAACGTGGCGATATTGATTTCAAAGATAAGATTGCAAACGCTAAAAAAGCT
GGTGCTGTAGGGGTCTTGATCTATGACAATCAAGACAAGGGCTTCCCGATTGAATTGCCAAATGTTGACCAG
ATGCCTGCGGCCTTTATCAGTCGAAGAGACGGTCTCTTATTAAAAGACAATCCCCCAAAAACCATTACCTTC
AATGCGACACCTAAGGTATTGCCAACAGCAAGTGGCACCAAACTAAGCCGCTTCTCAAGCTGGGGTCTGACA
GCTGACGGCAATATTAAACCGGATATTGCAGCACCCGGCCAAGATATTTTGTCATCAGTGGCTAACAACAAG
TATGCCAAACTTTCTGGAACTAGTATGTCTGCACCATTGGTAGCGGGTATCATGGGACTGTTGCAAAAGCAA
TATGAGACACAGTATCCTGATATGACACCATCAGAGCGTCTTGATTTAGCTAAGAAAGTATTGATGAGCTCA
GCAACTGCCCTATATGATGAAGATGAAAAAGCTTATTTTTCTCCTCGCCAACAGGGAGCAGGAGCAGTCGAT
GCTAAAAAAGCTTCAGCAGCAACGATGTATGTAACAGATAAGGACAATACCTCAAGCAAGGTTCACCTGAAC
AATGTTTCTGATAAATTTGAAGTAACAGTAACAGTCACAACAAATCTGATAAACCTCAAGAGTTGTATTAC
CAAGTAACTGTTCAAACAGATAAAGTAGATGGAAAACACTTTGCCTTGGCTCCTAAAGCATTGTATGAGACA
TCATGGCAAAAAATCACAATTCCAGCCAATAGCAGCAAACAAGTCACCGTTCCAATCGATGCTAGTCGATTT
AGCAAGGACTTGCTTGCCCAAATGAAAAATGGCTATTTCTTAGAAGGTTTTGTTCGTTTCAAACAAGATCCT
ACAAAAGAAGAGCTTATGAGCATTCCATATATTGGTTTCCGAGGTGATTTTGGCAATCTGTCAGCCTTAGAA
AAACCAATCTATGATAGCAAAGACGGTAGCAGCTACTATCATGAAGCAAATAGTGATGCCAAAGACCAATTA
GATGGTGATGGATTACAGTTTTACGCTCTGAAAAATAACTTTACAGCACTTACCACAGAGTCTAACCCATGG
ACGATTATTAAAGCTGTCAAAGAAGGGGTTGAAAACATAGAGGATATCGAATCTTCAGAGATCACAGAAACC

ATTTTTGCAGGTACTTTTGCAAAACAAGACGATGATAGCCACTACTATATCCACCGTCACGCTAATGGCAAA
CCATATGCTGCGATCTCTCCAAATGGGGACGGTAACAGAGATTATGTCCAATTCCAAGGTACTTTCTTGCGT
AATGCTAAAAACCTTGTGGCTGAAGTCTTGGACAAAGAAGGAAATGTTGTTTGGACAAGTGAGGTAACCGAG
CAAGTTGTTAAAAACTACAACAATGACTTGGCAAGCACACTTGGTTCAACCCGTTTTGAAAAAACGCGTTGG
GACGGTAAAGATAAAGACGGCAAAGTTGTTGCTAACGGAACCTACACCTATCGTGTTCGCTACACGCCGATT
AGCTCAGGTGCAAAAGAACAACACACTGATTTTGATGTGATTGTAGACAATACGACACCTGAAGTCGCAACA
TCGGCAACATTCTCAACAGAAGATAGTCGTTTGACACTTGCATCTAAACCAAAAACCAGCCAACCGGTTTAC
CGTGAGCGTATTGCTTACACTATATGGATGAGGATCTGCCAACAACAGAGTATATTTCTCCAAATGAAGAT
GGTACCTTTACTCTTCCTGAAGAGGCTGAAACAATGGAAGGCGCTACTGTTCCATTGAAAATGTCAGACTTT
ACTTATGTTGTTGAAGATATGGCTGGTAACATCACTTATACACCAGTGACTAAGCTATTGGAGGCCCACTCT
AATAAGCCAGAACAAGACGGTTCAGATCAAGCACCAGACAAGAAACCAGAAGCTAAACCAGAACAAGACGGT
TCAGGTCAAACACCAGATAAAAAAAAGAAACTAAACCAGAAAAAGATAGTTCAGGTCAAACACCAGGTAAA
ACTCCTCAAAAAGGTCAATCTTCTCGTACTCTAGAGAAACGATCTTCTAAGCGTGCTTTAGCTACAAAAGCA
TCAACAAGAGATCAGTTACCAACGACTAATGACAAGGATACAAATCGTTTACATCTCCTTAAGTTAGTTATG
ACCACTTTCTTCTTGGGA

SEQ ID NO. 26

MRKKQKLPFDKLAIALISTSILLNAQSDIKANTVTEDTPATEQAVEPPQPIAVSEESRSSKETKTSQTPSDV
GETVADDANDLAPQAPAKTADTPATSKATIRDLNDPSHVKTLQEKAGKGAGTVVAVIDAGFDKNHEAWRLTD
KTKARYQSKENLEKAKKEHGITYGEWVNDKVAYYHDYSKDGKNAVDQEHGTHVSGILSGNAPSEMKEPYRLE
GAMPEAQLLLMRVEIVNGLADYARNYAQAIRDAVNLGAKVINMSFGNAALAYANLPDETKKAFDYAKSKGVS
IVTSAGNDSSPGGKPRLPLADHPDYGVVGTPAAADSTLTVASYSPDKQLTETATVKTDDHQDKEMPVISTNR
FEPNKAYDYAYANRGTKEDDFKDVEGKIALIERGDIDFKDKIANAKKAGAVGVLIYDNQDKGFPIELPNVDQ
MPAAFISRRDGLLLKDNPPKTITFNATPKVLPTASGTKLSRPSSWGLTADGNIKPDIAAPGQDILSSVANNK
YAKLSGTSMSAPLVAGIMGLLQKQYETQYPDMTPSERLDLAKKVLMSSATALYDEDEKAYFSPRQQGAGAVD
AKKASAATMYVTDKDNTSSKVHLNNVSDKFEVTVTVHNKSDKPQELYYQVTVQTDKVDGKHFALAPKALYET
SWQKITIPANSSKQVTVPIDASRFSKDLLAQMKNGYFLEGFVRFKQDPTKEELMSIPYIGFRGDFGNLSALE
KPIYDSKDGSSYYHEANSDAKDQLDGDGLQFYALKNNFTALTTESNPWTIIKAVKEGVENIEDIESSEITET
IFAGTFAKQDDDSHYYIHRHANGKPYAAISPNGDGNRDYVQFQGTFLRNAKNLVAEVLDKEGNVVWTSEVTE
QVVKNYNNDLASTLGSTRFEKTRWDGKDKDGKVVANGTYTYRVRYTPISSGAKEQHTDFDVIVDNTTPEVAT
SATFSTEDSRLTLASKPKTSQPVYRERIAYTYMDEDLPTTEYISPNEDGTFTLPEEAETMEGATVPLKMSDF
TYVVEDMAGNITYPTVTKLLEGHSNKPEQDGSDQAPDKKPEAKPEQDGSGQTPDKKKETKPEKDSSGQTPGK
TPQKGQSSRTLEKRSSKRALATKASTRDQLPTTNDKDTNRLHLLKLVMTTFFLG

GBS 276 contains an N-terminal leader or signal sequence region which is indicated by the underlined sequence at the beginning of SEQ ID NO: 26 above. In one embodiment, one or more amino acids from the leader or signal sequence region of GBS 276 are removed. An example of such a GBS 276 fragment is set forth below as SEQ ID NO: 27.

SEQ ID NO: 27

QSDIKANTVTEDTPATEQAVEPPQPIAVSEESRSSKETKTSQTPSDVGETVADDANDLAPQAPAKTADTPAT
SKATIRDLNDPSHVKTLQEKAGKGAGTVVAVIDAGFDKNHEAWRLTDKTKARYQSKENLEKAKKEHGITYGE
WVNDKVAYYHDYSKDGKNAVDQEHGTHVSGILSGNAPSEMKEPYRLEGAMPEAQLLLMRVEIVNGLADYARN
YAQAIRDAVNLGAKVINMSFGNAALAYANLPDETKKAFDYAKSKGVSIVTSAGNDSSFGGKPRLPLADHPDY
GVVGTPAAADSTLTVASYSPDKQLTETATVKTDDHQDKEMPVISTNRFEPNKAYDYAYANRGTKEDDFKDVE
GKIALIERGDIDFKDKIANAKKAGAVGVLIYDNQDKGFPIELPNVDQMPAAFISRRDGLLLKDNPPKTITFN
ATPKVLPTASGTKLSRFSSWGLTADGNIKPDIAAPGQDILSSVANNKYAKLSGTSMSAPLVAGIMGLLQKQY
ETQYPDMTPSERLDLAKKVLMSSATALYDEDEKAYFSPRQQGAGAVDAKKASAATMYVTDKDNTSSKVHLNN
VSDKFEVTVTVHNKSDKPQELYYQVTVQTDKVDGKHFALAPKALYETSWQKITIPANSSKQVTVPIDASRFS
KDLLAQMKNGYFLEGFVRFKQDPTKEELMSIPYIGFRGDFGNLSALEKPIYDSKDGSSYYHEANSDAKDQLD
GDGLQFYALKNNFTALTTESNPWTIIKAVKEGVENIEDIESSEITETIFAGTFAKQDDDSHYYIHRHANGKP
YAAISPNGDGNRDYVQFQGTFLRNAKNLVAEVLDKEGNVVWTSEVTEQVVKNYNNDLASTLGSTRFEKTRWD
GKDKDGKVVANGTYTYRVRYTPISSGAKEQHTDFDVIVDNTTPEVATSATFSTEDSRLTLASKPKTSQPVYR
ERIAYTYMDEDLPTTEYISPNEDGTFTLPEEAETMEGATVPLKMSDFTYVVEDMAGNITYTPVTKLLEGHSN

KPEQDGSDQAPDKKPEAKPEQDGSGQTPDKKKETKPEKDSSGQTPGKTPQKGQSSRTLEKRSSKRALATKAS
TRDQLPTTNDKDTNRLHLLKLVMTTFFLG

GBS 276 contains a C-terminal transmembrane and/or cytoplasmic region which is indicated by the underlined sequence near the end of SEQ ID NO: 26 above. In one embodiment, one or more amino acids from the transmembrane or cytoplasmic regions of GBS 276 are removed. An example of such a GBS 276 fragment is set forth below as SEQ ID NO: 28.

SEQ ID NO: 28

MRKKQKLPFDKLAIALISTSILLNAQSDIKANTVTEDTPATEQAVEPPQPIAVSEESRSSKETKTSQTPSDV
GETVADDANDLAPQAPAKTADTPATSKATIRDLNDPSHVKTLQEKAGKGAGTVVAVIDAGFDKNHEAWRLTD
KTKARYQSKENLEKAKKEHGITYGEWVNDKVAYYHDYSKDGKNAVDQEHGTHVSGILSGNAPSEMKEPYRLE
GAMPEAQLLLMRVEIVNGLADYARNYAQAIRDAVNLGAKVINMSFGNAALAYANLPDETKKAFDYAKSKGVS
IVTSAGNDSSFGGKPRLPLADHPDYGVVGTPAAADSTLTVASYSPDKQLTETATVKTDDHQDKEMPVISTNR
FEPNKAYDYAYANRGTKEDDFKDVEGKIALIERGDIDFKDKIANAKKAGAVGVLIYDNQDKGFPIELPNVDQ
MPAAFISRRDGLLLKDNPPKTITFNATPKVLPTASGTKLSRFSSWGLTADGNIKPDIAAPGQDILSSVANNK
YAKLSGTSMSAPLVAGIMGLLQKQYETQYPDMTPSERLDLAKKVLMSSATALYDEDEKAYFSPRQQGAGAVD
AKKASAATMYVTDKDNTSSKVHLNNVSDKFEVTVTVHNKSDKPQELYYQVTVQTDKVDGKHFALAPKALYET
SWQKITIPANSSKQVTVPIDASRFSKDLLAQMKNGYFLEGFVRFKQDPTKEELMSIPYIGFRGDFGNLSALE
KPIYDSKDGSSYIHEANSDAKDQLDGDGLQFYALKNNPTALTTESNPWTIIKAVKEGVENIEDIESSEITET
IFAGTPAKQDDDSHYYIHRHANGKPYAAISPNGDGNRDYVQFQGTPLRNAKNLVAEVLDKEGNVVWTSEVTE
QVVKNYNNNDLASTLGSTRFEKTRWDGKDKDGKVVANGTYTYRVRYTPISSGAKEQHTDFDVIVDNTTPEVAT
SATFSTEDSRLTLASKPKTSQPVYRERIAYTYMDEDLPTTEYISPNEDGTFTLPEEAETMEGATVPLKMSDF
TYVVEDMAGNITYTPVTKLLEGHSNKPEQDGSDQAPDKKPEAKPEQDGSGQTPDKKKETKPEKDSSGQTPGK
TPQKGQSSRTLEKRSSKRALATK

In one embodiment, one or more amino acids from the leader or signal sequence region and one or more amino acids from the transmembrane or cytoplasmic regions of GBS 276 are removed. An example of such a GBS 276 fragment is set forth below as SEQ ID NO: 29.

SEQ ID NO: 29

QSDIKANTVTEDTPATEQAVEPPQPIAVSEESRSSKETKTSQTPSDVGETVADDANDLAPQAPAKTADTPAT
SKATIRDLNDPSHVKTLQEKAGKGAGTVVAVIDAGFDKNHEAWRLTDKTKARYQSKENLEKAKKEHGITYGE
WVNDKVAYYHDYSKDGKNAVDQEHGTHVSGILSGNAPSEMKEPYRLEGAMPEAQLLLMRVEIVNGLADYARN
YAQAIRDAVNLGAKVINMSFGNAALAYANLPDETKKAFDYAKSKGVSIVTSAGNDSSFGGKPRLPLADHPDY
GVVGTPAAADSTLTVASYSPDKQLTETATVKTDDHQDKEMPVISTNRFEPNKAYDYAYANRGTKEDDFKDVE
GKIALIERGDIDFKDKIANAKKAGAVGVLIYDNQDKGFPIELPNVDQMPAAFISRRDGLLLKDNPPKTITFN
ATPKVLPTASGTKLSRFSSWGLTADGNIKPDIAAPGQDILSSVANNKYAKLSGTSMSAPLVAGIMGLLQKQY
ETQYPDMTPSERLDLAKKVLMSSATALYDEDEKAYFSPRQQGAGAVDAKKASAATMYVTDKDNTSSKVHLNN
VSDKFEVTVTVHNKSDKPQELYYQVTVQTDKVDGKHFALAPKALYETSWQKITIPANSSKQVTVPIDASRFS
KDLLAQMKNGYFLEGFVRFKQDPTKEELMSIPYIGFRGDFGNLSALEKPIYDSKDGSSYIHEANSDAKDQLD
GDGLQFYALKNNFTALTTESNPWTIIKAVKEGVENIEDIESSEITETIFAGTPAKQDDDSHYYIHRHANGKP
YAAISPNGDGNRDYVQFQGTFLRNAKNLVAEVLDKEGNVVWTSEVTEQVVKNYNNDLASTLGSTRFEKTRWD
GKDKDGKVVANGTYTYRVRYTPISSGAKEQHTDFDVIVDNTTPEVATSATFSTEDSRLTLASKPKTSQPVYR
ERIAYTYMDEDLPTTEYISPNEDGTFTLPEEAETMEGATVPLKMSDFTYVVEDMAGNITYTPVTKLLEGHSN
KPEQDGSDQAPDKKPEAKPEQDGSGQTPDKKKETKPEKDSSGQTPGKTPQKGQSSRTLEKRSSKRALATK

Further description of GBS 276 can be found in the following references: Qi Chen et al., "Immunization with C5a Peptidase or Peptidase-Type III Polysaccharide conjugate Vaccines Enhances Clearance of Group B Streptococci from Lungs of Infected Mice", Infection and Immunity (2002) 70 (11):6409 – 6415; Beckmann et al., "Identification of Novel Adhesions from Group B Streptococci by Use of Phage Display Reveals that C5a Peptidase Mediates Fibronectin Binding" Infection and Immunity (2002)

70(6):2869 – 2876; Cheng et al., "The Group B Streptococcal C5a Peptidase Is Both a Specific Protease and an Invasin" Infection and Immunity (2002) 70(5) 2408 – 2413; and Cheng et al., "Antibody against Surface-Bound C5a Peptidase Is Opsonic and Initiates Macrophage Killing of Group B Streptococci" Infection and Immunity (2001) 69(4):2302 – 2308.

GBS 305

GBS 305 refers to a UDP-N-acetylmuramoylalanine--D-glutamate ligase, also referred to as Mur D. Nucleotide and amino acid sequences of GBS 305 sequenced from serotype V isolated strain 2603 V/R are set forth in Ref. 3 as SEQ ID 207 and SEQ ID 208. These sequences are set forth below as SEQ ID NOS 30 and 31:

SEQ ID NO. 30

ATGGGACGAGTAATGAAAACAATAACAACATTTGAAAATAAAAAAGTTTTAGTCCTTGGTTTAGCACGATCT
GGAGAAGCTGCTGCACGTTTGTTAGCTAAGTTAGGAGCAATAGTGACAGTTAATGATGGCAAACCATTTGAT
GAAAATCCAACAGCACAGTCTTTGTTGGAAGAGGGTATTAAAGTGGTTTGTGGTAGTCATCCTTTAGAATTG
TTAGATGAGGATTTTTGTTACATGATTAAAAATCCAGGAATACCTTATAACAATCCTATGGTCAAAAAAGCA
TTAGAAAAACAAATCCCTGTTTTGACTGAAGTGGAATTAGCATACTTAGTTTCAGAATCTCAGCTAATAGGT
ATTACAGGCTCTAACGGGAAAACGACAACGACAACGATGATTGCAGAAGTCTTAAATGCTGGAGGTCAGAGA
GGTTTGTTAGCTGGGAATATCGGCTTTCCTGCTAGTGAAGTTGTTCAGGCTGCGAATGATAAAGATACTCTA
GTTATGGAATTATCAAGTTTTCAGCTAATGGGAGTTAAGGAATTTCGTCCTCATATTGCAGTAATTACTAAT
TTAATGCCAACTCATTTAGATTATCATGGGTCTTTTGAAGATTATGTTGCTGCAAAATGGAATATCCAAAAT
CAAATGTCTTCATCTGATTTTTTGGTACTTAATTTTAATCAAGGTATTTCTAAAGAGTTAGCTAAAACTACT
AAAGCAACAATCGTTCCTTTCTCTACTACGGAAAAAGTTGATGGTGCTTACGTACAAGACAAGCAACTTTTC
TATAAAGGGGAGAATATTATGTCAGTAGATGACATTGGTGTCCCAGGAAGCCATAACGTAGAGAATGCTCTA
GCAACTATTGCGGTTGCTAAACTGGCTGGTATCAGTAATCAAGTTATTAGAGAAACTTTAAGCAATTTTGGA
GGTGTTAAACACCGCTTGCAATCACTCGGTAAGGTTCATGGTATTAGTTTCTATAACGACAGCAAGTCAACT
AATATATTGGCAACTCAAAAAGCATTATCTGGCTTTGATAATACTAAAGTTATCCTAATTGCAGGAGGTCTT
GATCGCGGTAATGAGTTTGATGAATTGATACCAGATATCACTGGACTTAAACATATGGTTGTTTTAGGGGAA
TCGGCATCTCGAGTAAAACGTGCTGCACAAAAAGCAGGAGTAACTTATAGCGATGCTTTAGATGTTAGAGAT
GCGGTACATAAAGCTTATGAGGTGGCACAACAGGGCGATGTTATCTTGCTAAGTCCTGCAAATGCATCATGG
GACATGTATAAGAATTTCGAAGTCCGTGGTGATGAATTCATTGATACTTTCGAAAGTCTTAGAGGAGAG

SEQ ID NO. 31

MGRVMKTITTFENKKVLVLGLARSGEAAARLLAKLGAIVTVNDGKPFDENPTAQSLLEEGIKVVCGSHPLEL
LDEDFCYMIKNPGIPYNNPMVKKALEKQIPVLTEVELAYLVSESQLIGITGSNGKTTTTMIAEVLNAGGQR
GLLAGNIGFPASEVVQAANDKDTLVMELSSFQLMGVKEFRPHIAVITNLMPTHLDYHGSFEDYVAAKWNIQN
QMSSSDFLVLNFNQGISKELAKTTKATIVPFSTTEKVDGAYVQDKQLFYKGENIMSVDDIGVPGSHNVENAL
ATIAVAKLAGISNQVIRETLSNFGGVKHRLQSLGKVHGISFYNDSKSTNILATQKALSGFDNTKVILIAGGL
DRGNEFDELIPDITGLKHMVVLGESASRVKRAAQKAGVTYSDALDVRDAVHKAYEVAQQGDVILLSPANASW
DMYKNFEVRGDEFIDTFESLRGE

GBS 305 contains an N-terminal leader or signal sequence region which is indicated by the underlined sequence at the beginning of SEQ ID NO: 31 above. In one embodiment, one or more amino acids from the leader or signal sequence region are removed from GBS 305. An example of such a GBS 305 fragment is set forth below as SEQ ID NO: 32.

SEQ ID NO: 32

ITTFENKKVLVLGLARSGEAAARLLAKLGAIVTVNDGKPFDENPTAQSLLEEGIKVVCGSHPLELLDEDFCY
MIKNPGIPYNNPMVKKALEKQIPVLTEVELAYLVSESQLIGITGSNGKTTTTTMIAEVLNAGGQRGLLAGNI
GFPASEVVQAANDKDTLVMELSSFQLMGVKEFRPHIAVITNLMPTHLDYHGSFEDYVAAKWNIQNQMSSSDF
LVLNFNQGISKELAKTTKATIVPFSTTEKVDGAYVQDKQLFYKGENIMSVDDIGVPGSHNVENALATIAVAK

LAGISNQVIRETLSNFGGVKHRLQSLGKVHGISFYNDSKSTNILATQKALSGFDNTKVILIAGGLDRGNEFD
ELIPDITGLKHMVVLGESASRVKRAAQKAGVTYSDALDVRDAVHKAYEVAQQGDVILLSPANASWDMYKNFE
VRGDEFIDTFESLRGE

GBS 305 contains a C-terminal transmembrane or cytoplasmic region indicated by the underlined sequence near the end of SEQ ID NO: 31 above. In one embodiment, one or more amino acids from the transmembrane or cytomplasmic regions are removed from GBS 305. An example of such a GBS 305 fragment is set forth below as SEQ ID NO: 33.

SEQ ID NO: 33

MGRVMKTITTFENKKVLVLGLARSGEAAARLLAKLGAIVTVNDGKPFDENPTAQSLLEEGIKVVCGSHPLEL
LDEDFCYMIKNPGIPYNNPMVKKALEKQIPVLTEVELAYLVSESQLIGITGSNGKTTTTMIAEVLNAGGQR
GLLAGNIGFPASEVVQAANDKDTLVMELSSFQLMGVKEFRPHIAVITNLMPTHLDYHGSFEDYVAAKWNIQN
QMSSSDFLVLNFNQGISKELAKTTKATIVPFSTTEKVDGAYVQDKQLFYKGENIMSVDDIGVPGSHNVENAL
ATIAVAKLAGISNQVIRETLSNFGGVKHRLQSLGKVHGISFYNDSK

In one embodiment one or more amino acids from the leader or signal sequence region and one or more amino acids from the transmembrane or cytoplasmic regions are removed from GBS 305. An example of such a GBS 305 fragment is set forth below as SEQ ID NO: 34.

SEQ ID NO: 34

ITTFENKKVLVLGLARSGEAAARLLAKLGAIVTVNDGKPFDENPTAQSLLEEGIKVVCGSHPLELLDEDFCY
MIKNPGIPYNNPMVKKALEKQIPVLTEVELAYLVSESQLIGITGSNGKTTTTMIAEVLNAGGQRGLLAGNI
GFPASEVVQAANDKDTLVMELSSFQLMGVKEFRPHIAVITNLMPTHLDYHGSFEDYVAAKWNIQNQMSSSDF
LVLNFNQGISKELAKTTKATIVPFSTTEKVDGAYVQDKQLFYKGENIMSVDDIGVPGSHNVENALATIAVAK
LAGISNQVIRETLSNFGGVKHRLQSLGKVHGISFYNDSK

GBS 322

GBS 322 refers to a surface immunogenic protein, also referred to as "sip". Nucleotide and amino acid sequences of GBS 322 sequenced from serotype V isolated strain 2603 V/R are set forth in Ref. 3 as SEQ ID 8539 and SEQ ID 8540. These sequences are set forth below as SEQ ID NOS 35 and 36:

SEQ ID NO. 35

ATGAATAAAAAGGTACTATTGACATCGACAATGGCAGCTTCGCTATTATCAGTCGCAAGTGTTCAAGCACAA
GAAACAGATACGACGTGGACAGCACGTACTGTTTCAGAGGTAAAGGCTGATTTGGTAAAGCAAGACAATAAA
TCATCATATACTGTGAAATATGGTGATACACTAAGCGTTATTTCAGAAGCAATGTCAATTGATATGAATGTC
TTAGCAAAAATAAATAACATTGCAGATATCAATCTTATTTATCCTGAGACAACACTGACAGTAACTTACGAT
CAGAAGAGTCATACTGCCACTTCAATGAAAATAGAAACACCAGCAACAAATGCTGCTGGTCAAACAACAGCT
ACTGTGGATTTGAAAACCAATCAAGTTTCTGTTGCAGACCAAAAAGTTTCTCTCAATACAATTTCGGAAGGT
ATGACACCAGAAGCAGCAACAACGATTGTTTCGCCAATGAAGACATATTCTTCTGCGCCAGCTTTGAAATCA
AAAGAAGTATTAGCACAAGAGCAAGCTGTTAGTCAAGCAGCAGCTAATGAACAGGTATCACCAGCTCCTGTG
AAGTCGATTACTTCAGAAGTTCCAGCAGCTAAAGAGGAAGTTAAACCAACTCAGACGTCAGTCAGTCAGTCA
ACAACAGTATCACCAGCTTCTGTTGCCGCTGAAACACCAGCTCCAGTAGCTAAAGTAGCACCGGTAAGAACT
GTAGCAGCCCCTAGAGTGGCAAGTGTTAAAGTAGTCACTCCTAAAGTAGAAACTGGTGCATCACCAGAGCAT
GTATCAGCTCCAGCAGTTCCTGTGACTACGACTTCACCAGCTACAGACAGTAAGTTACAAGCGACTGAAGTT
AAGAGCGTTCCGGTAGCACAAAAAGCTCCAACAGCAACACCGGTAGCACAACCAGCTTCAACAACAAATGCA
GTAGCTGCACATCCTGAAAATGCAGGGCTCCAACCTCATGTTGCAGCTTATAAAGAAAAAGTAGCGTCAACT
ATGGAGTTAATGAATTCAGTACATACCGTGCGGGAGATCCAGGTGATCATGGTAAAGGTTTAGCAGTTGAC
TTTATTGTAGGTACTAATCAAGCACTTGGTAATAAAGTTGCACAGTACTCTACACAAAATATGGCAGCAAAT
AACATTTCATATGTTATCTGGCAACAAAAGTTTTACTCAAATACAAACAGTATTTATGGACCTGCTAATACT
TGGAATGCAATGCCAGATCGTGGTGGCGTTACTGCCAACCACTATGACCACGTTCACGTATCATTTAACAAA
TAATATAAAAAAGGAAGCTATTTGGCTTCTTTTTTATATGCCTTGAATAGACTTTCAAGGTTCTTATATAAT
TTTTATTA

SEQ ID NO. 36

MNKKVLLTSTMAASLLSVASVQAQETDTTWTARTVSEVKADLVKQDNKSSYTVKYGDTLSVISEAMSIDMNV
LAKINNIADINLIYPETTLTVTYDQKSHTATSMKIETPATNAAGQTTATVDLKTNQVSVADQKVSLNTISEG
MTPEAATTIVSPMKTYSSAPALKSKEVLAQEQAVSQAAANEQVSPAPVKSITSEVPAAKEEVKPTQTSVSQS
TTVSPASVAAETPAPVAKVAPVRTVAAPRVASVKVVTPKVETGASPEHVSAPAVPVTTTSPATDSKLQATEV
KSVPVAQKAPTATPVAQPASTTNAVAAHPENAGLQPHVAAYKEKVASTYGVNEFSTYRAGDPGDHGKGLAVD
FIVGTNQALGNKVAQYSTQNMAANNISYVIWQQKFYSNTNSIYGPANTWNAMPDRGGVTANHYDHVHVSFNK

GBS 322 contains an N-terminal leader or signal sequence region which is indicated by the underlined sequence near the beginning of SEQ ID NO: 36. In one embodiment, one or more amino acids from the leader or signal sequence region of GBS 322 are removed. An example of such a GBS 322 fragment is set forth below as SEQ ID NO: 37.

SEQ ID NO: 37

DLVKQDNKSSYTVKYGDTLSVISEAMSIDMNVLAKINNIADINLIYPETTLTVTYDQKSHTATSMKIETPAT
NAAGQTTATVDLKTNQVSVADQKVSLNTISEGMTPEAATTIVSPMKTYSSAPALKSKEVLAQEQAVSQAAAN
EQVSPAPVKSITSEVPAAKEEVKPTQTSVSQSTTVSPASVAAETPAPVAKVAPVRTVAAPRVASVKVVTPKV
ETGASPEHVSAPAVPVTTTSPATDSKLQATEVKSVPVAQKAPTATPVAQPASTTNAVAAHPENAGLQPHVAA
YKEKVASTYGVNEFSTYRAGDPGDHGKGLAVDFIVGTNQALGNKVAQYSTQNMAANNISYVIWQQKFYSNTN
SIYGPANTWNAMPDRGGVTANHYDHVHVSFNK

GBS 330

GBS 330 refers to a pyruvate kinase, also referred to as "pyk". Nucleotide and amino acid sequences of GBS 330 sequenced from serotype V isolated strain 2603 V/R are set forth in Ref. 3 as SEQ ID 8791 and SEQ ID 8792. These sequences are set forth below as SEQ ID NOS 38 and 39:

SEQ ID NO. 38

ATGAATAAACGCGTAAAAATCGTTGCAACACTTGGTCCTGCGGTTGAATTCCGTGGTGGTAAGAAGTTTGGT
GAGTCTGGATACTGGGGTGAAAGCCTTGACGTAGAAGCTTCAGCAGAAAAAATTGCTCAATTGATTAAAGAA
GGTGCTAACGTTTTCCGTTTCAACTTCTCACATGGAGATCATGCTGAGCAAGGAGCTCGTATGGCTACTGTT
CGTAAAGCAGAAGAGATTGCAGGACAAAAAGTTGGCTTCCTCCTTGATACTAAAGGACCTGAAATTCGTACA
GAACTTTTTGAAGATGGTGCAGATTTCCATTCATATACAACAGGTACAAAATTACGTGTTGCTACTAAGCAA
GGTATCAAATCAACTCCAGAAGTGATTGCATTGAATGTTGCTGGTGGACTTGACATCTTTGATGACGTTGAA
GTTGGTAAGCAAATCCTTGTTGATGATGGTAAACTAGGTCTTACTGTGTTTGCAAAAGATAAAGACACTCGT
GAATTTGAAGTAGTTGTTGAGAATGATGGCCTTATTGGTAAACAAAAAGGTGTAAACATCCCTTATACTAAA
ATTCCTTTCCCAGCACTTGCAGAACGCGATAATGCTGATATCCGTTTTGGACTTGAGCAAGGACTTAACTTT
ATTGCTATCTCATTTGTACGTACTGCTAAAGATGTTAATGAAGTTCGTGCTATTTGTGAAGAAACTGGSMAT
GGACACGTTAAGTTGTTTGCTAAAATTGAAAATCAACAAGGTATCGATAATATTGATGAGATTATCGAAGCA
GCAGATGGTATTATGATTGCTCGTGGTGATATGGGTATCGAAGTTCCATTTGAAATGGTTCCAGTTTACCAA
AAAATGATCATTACTAAAGTTAATGCAGCTGGTAAAGCAGTTATTACAGCAACAAATATGCTTGAAACAATG
ACTGATAAACCACGTGCGACTCGTTCAGAAGTATCTGATGTCTTCAATGCTGTTATTGATGGTACTGATGCT
ACAATGCTTTCAGGTGAGTCAGCTAATGGTAAATACCCAGTTGAGTCAGTTCGTACAATGGCTACTATTGAT
AAAAATGCTCAAACATTACTCAATGAGTATGGTCGCTTAGACTCATCTGCATTCCCACGTAATAACAAAACT
GATGTTATTGCATCTGCGGTTAAAGATGCAACACACTCAATGGATATCAAACTTGTTGTAACAATTACTGAA
ACAGGTAATACAGCTCGTGCCATTTCTAAATTCCGTCCAGATGCAGACATTTTGGCTGTTACATTTGATGAA
AAAGTACAACGTTCATTGATGATTAACTGGGGTGTTATCCCTGTCCTTGCAGACAAACCAGCATCTACAGAT
GATATGTTTGAGGTTGCAGAACGTGTAGCACTTGAAGCAGGATTTGTTGAATCAGGCGATAATATCGTTATC
GTTGCAGGTGTTCCTGTAGGTACAGGTGGAACTAACACAATGCGTGTTCGTACTGTTAAA

SEQ ID NO. 39

MNKRVKIVATLGPAVEFRGGKKPGESGYWGESLDVEASAEKIAQLIKEGANVFRFNFSHGDHAEQGARMATV
RKAEEIAGQKVGFLLDTKGPEIRTELFEDGADFHSYTTGTKLRVATKQGIKSTPEVIALNVAGGLDIFDDVE
VGKQILVDDGKLGLTVFAKDKDTREFEVVVENDGLIGKQKGVNIPYTKIPFPALAERDNADIRFGLEQGLNF

IAISFVRTAKDVNEVRAICEETGXGHVKLFAKIENQQGIDNIDEIIEAADGIMIARGDMGIEVPFEMVPVYQ
KMIITKVNAAGKAVITATNMLETMTDKPRATRSEVSDVFNAVIDGTDATMLSGESANGKYPVESVRTMATID
KNAQTLLNEYGRLDSSAFPRNNKTDVIASAVKDATHSMDIKLVVTITETGNTARAISKFRPDADILAVTFDE
KVQRSLMINWGVIPVLADKPASTDDMFEVAERVALEAGFVESGDNIVIVAGVPVGTGGTNTMRVRTVK

GBS 338

GBS 338 refers to a Sat D protein. Nucleotide and amino acid sequences of GBS 338 sequenced from serotype V isolated strain 2603 V/R are set forth in Ref. 3 as SEQ ID 8637 and SEQ ID 8638. These sequences are set forth below as SEQ ID NOS 40 and 41:

SEQ ID NO. 40
TTGTCTGCTATAATAGACAAAAAGGTGGTGATATTTATGTATTTAGCATTAATCGGTGATATCATTAATTCA
AAACAGATACTTGAACGTGAAACTTTCCAACAGTCTTTTCAGCAACTAATGACCGAACTATCTGATGTATAT
GGTGAAGAGCTGATTTCTCCATTCACTATTACAGCTGGTGATGAATTTCAAGCTTTATTGAAACCATCAAAA
AAGGTATTTCAAATTATTGACCATATTCAACTAGCTCTAAAACCTGTTAATGTAAGGTTCGGCCTCGGTACA
GGAAACATTATAACATCCATCAATTCAAATGAAAGTATCGGTGCTGATGGTCCTGCCTACTGGCATGCTCGC
TCAGCTATTAATCATATACATGATAAAAATGATTATGGAACAGTTCAAGTAGCTATTTGCCTTGATGATGAA
GACCAAAACCTTGAATTAACACTAAATAGTCTCATTTCAGCTGGTGATTTTATCAAGTCAAAATGGACTACA
AACCATTTTCAAATGCTTGAGCACTTAATACTTCAAGATAATTATCAAGAACAATTTCAACATCAAAAGTTA
GCCCAACTGGAAAATATTGAACCTAGTGCGCTGACTAAACGCCTTAAAGCAAGCGGTCTGAAGATTTACTTA
AGAACGAGAACACAGGCAGCCGATCTATTAGTTAAAAGTTGCACTCAAACTAAAGGGGGAAGCTATGATTTC

SEQ ID NO. 41
MSAIIDKKVVIFMYLALIGDIINSKQILERETFQQSFQQLMTELSDVYGEELISPFTITAGDEFQALLKPSK
KVFQIIDHIQLALKPVNVRFGLGTGNIITSINSNESIGADGPAYWHARSAINHIHDKNDYGTVQVAICLDDE
DQNLELTLNSLISAGDFIKSKWTTNHFQMLEHLILQDNYQEQFQHQKLAQLENIEPSALTKRLKASGLKIYL
RTRTQAADLLVKSCTQTKGGSYDF

GBS 338 may contain an N-terminal leader or signal sequence region which is indicated by the underlined sequence at the beginning of SEQ ID NO: 41 above. In one embodiment, one or more amino acids from the leader or signal sequence region are removed from GBS 338. An example of such a GBS 338 fragment is set forth below as SEQ ID NO: 42.

SEQ ID NO: 42
MYLALIGDIINSKQILERETFQQSFQQLMTELSDVYGEELISPFTITAGDEFQALLKPSKKVFQIIDHIQLA
LKPVNVRFGLGTGNIITSINSNESIGADGPAYWHARSAINHIHDKNDYGTVQVAICLDDEDQNLELTLNSLI
SAGDFIKSKWTTNHFQMLEHLILQDNYQEQFQHQKLAQLENIEPSALTKRLKASGLKIYLRTRTQAADLLVK
SCTQTKGGSYDF

GBS 361

GBS 361 refers to a cylI protein. Nucleotide and amino acid sequences of GBS 361 sequenced from serotype V isolated strain 2603 V/R are set forth in Ref. 3 as SEQ ID 8769 and SEQ ID 8770. These sequences are set forth below as SEQ ID NOS 43 and 44:

SEQ ID NO. 43
ATGAGCGTATATGTTAGTGGAATAGGAATTATTTCTTCTTTGGGAAAGAATTATAGCGAGCATAAACAGCAT
CTCTTCGACTTAAAAGAAGGAATTTCTAAACATTTATATAAAAATCACGACTCTATTTTAGAATCTTATACA
GGAAGCATAACTAGTGACCCAGAGGTTCCTGAGCAATACAAAGATGAGACACGTAATTTTAAATTTGCTTTT
ACCGCTTTTGAAGAGGCTCTTGCTTCTTCAGGTGTTAATTTAAAAGCTTATCATAATATTGCTGTGTGTTTA
GGGACCTCACTTGGGGGAAAGAGTGCTGGTCAAAATGCCTTGTATCAATTTGAAGAAGGAGAGCGTCAAGTA
GATGCTAGTTTATTAGAAAAAGCATCTGTTTACCATATTGCTGATGAATTGATGGCTTATCATGATATTGTG
GGAGCTTCGTATGTTATTTCAACCGCCTGTTCTGCAAGTAATAATGCCGTAATATTAGGAACACAATTACTT

CAAGATGGCGATTGTGATTTAGCTATTTGTGGTGGCTGTGATGAGTTAAGTGATATTTCTTTAGCAGGCTTC
ACATCACTAGGAGCTATTAATACAGAAATGGCATGTCAGCCCTATTCTTCTGGAAAAGGAATCAATTTGGGT
GAGGGCGCTGGTTTTGTTGTTCTTGTCAAAGATCAGTCCTTAGCTAAATATGGAAAAATTATCGGTGGTCTT
ATTACTTCAGATGGTTATCATATAACAGCACCTAAGCCAACAGGTGAAGGGGCGGCACAGATTGCAAAGCAG
CTAGTGACTCAAGCAGGTATTGACTACAGTGAGATTGACTATATTAACGGTCACGGTACAGGTACTCAAGCT
AATGATAAAATGGAAAAAAATATGTATGGTAAGTTTTTCCCGACAACGACATTGATCAGCAGTACCAAGGGG
CAAACGGGTCATACTCTAGGGGCTGCAGGTATTATCGAATTGATTAATTGTTTAGCGGCAATAGAGGAACAG
ACTGTACCAGCAACTAAAAATGAGATTGGGATAGAAGGTTTTCCAGAAAATTTTGTCTATCATCAAAAGAGA
GAATACCCAATAAGAAATGCTTTAAATTTTTCGTTTGCTTTTGGTGGAAATAATAGTGGTGTCTTATTGTCA
TCTTTAGATTCACCTCTAGAAACATTACCTGCTAGAGAAATCTTAAAATGGCTATCTTATCATCTGTTGCT
TCCATTTCTAAGAATGAATCACTTTCTATAACCTATGAAAAAGTTGCTAGTAATTTCAACGACTTTGAAGCA
TTACGCTTTAAAGGGGCTAGACCACCCAAAACTGTCAACCCAGCACAATTTAGGAAAATGGATGATTTTTCC
AAAATGGTTGCCGTAACAACAGCTCAAGCACTAATAGAAAGCAATATTAATCTAAAAAAACAAGATACTTCA
AAAGTAGGAATTGTATTTACAACACTTTCTGGACCAGTTGAGGTTGTTGAAGGTATTGAAAGCAAATCACA
ACAGAAGGATATGCACATGTTTCTGCTTCACGATTCCCGTTTACAGTAATGAATGCAGCAGCTGGTATGCTT
TCTATCATTTTTAAAATAACAGGTCCTTTATCTGTCATTTCGACAAATAGTGGAGCGCTTGATGGTATACAA
TATGCCAAGGAAATGATGCGTAACGATAATCTAGACTATGTGATTCTTGTTTCTGCTAATCAGTGGACAGAC
ATGAGTTTTATGTGGTGGCAACAATTAAACTATGATAGTCAAATGTTTGTCGGTTCTGATTATTGTTCAGCA
CAAGTCCTCTCTCGTCAAGCATTGGATAATTCTCCTATAATATTAGGTAGTAAACAATTAAAATATAGCCAT
AAAACATTCACAGATGTGATGACTATTTTTGATGCTGCGCTTCAAAATTTATTATCAGACTTAGGACTAACC
ATAAAAGATATCAAAGGTTTCGTTTGGAATGAGCGGAAGAAGGCAGTTAGTTCAGATTATGATTTCTTAGCG
AACTTGTCTGAGTATTATAATATGCCAAACCTTGCTTCTGGTCAGTTTGGATTTTCATCTAATGGTGCTGGT
GAAGAACTGGACTATACTGTTAATGAAAGTATAGAAAAGGGCTATTATTTAGTCCTATCTTATTCGATCTTC
GGTGGTATCTCTTTTGCTATTATTGAAAAAAGG

SEQ ID NO. 44

MSVYVSGIGIISSLGKNYSEHKQHLFDLKEGISKHLYKNHDSILESYTGSITSDPEVPEQYKDETRNFKFAF
TAFEEALASSGVNLKAYHNIAVCLGTSLGGKSAGQNALYQFEEGERQVDASLLEKASVYHIADELMAYHDIV
GASYVISTACSASNNAVILGTQLLQDGDCDLAICGGCDELSDISLAGFTSLGAINTEMACQPYSSGKGINLG
EGAGFVVLVKDQSLAKYGKIIGGLITSDGYHITAPKPTGEGAAQIAKQLVTQAGIDYSEIDYINGHGTGTQA
NDKMEKNMYGKFPFTTTLISSTKGQTGHTLGAAGIIELINCLAAIEEQTVPATKNEIGIEGFPENFVYHQKR
EYPIRNALNFSFAFGGNNSGVLLSSLDSPLETLPARENLKMAILSSVASISKNESLSITYEKVASNFNDFEA
LRFKGARPPKTVNPAQFRKMDDFSKMVAVTTAQALIESNINLKKQDTSKVGIVFTTLSGPVEVVEGIEKQIT
TEGYAHVSASRFPFTVMNAAAGMLSIIFKITGPLSVISTNSGALDGIQYAKEMMRNDNLDYVILVSANQWTD
MSFMWWQQLNYDSQMFVGSDYCSAQVLSRQALDNSPIILGSKQLKYSHKTFTDVMTIFDAALQNLLSDLGLT
IKDIKGFVWNERKKAVSSDYDFLANLSEYYNMPNLASGQFGFSSNGAGEELDYTVNESIEKGYYLVLSYSIF
GGISFAIIEKR

GBS 361 may contain an N-terminal leader or signal sequence region which is indicated by the underlined sequence at the beginning of SEQ ID NO: 44 above. In one embodiment, one or more amino acids from the leader or signal sequence region are removed from GBS 361. An example of such a GBS 361 fragment is set forth below as SEQ ID NO: 45.

SEQ ID NO: 45

VSGIGIISSLGKNYSEHKQHLFDLKEGISKHLYKNHDSILESYTGSITSDPEVPEQYKDETRNFKFAFTAFE
EALASSGVNLKAYHNIAVCLGTSLGGKSAGQNALYQFEEGERQVDASLLEKASVYHIADELMAYHDIVGASY
VISTACSASNNAVILGTQLLQDGDCDLAICGGCDELSDISLAGFTSLGAINTEMACQPYSSGKGINLGEGAG
FVVLVKDQSLAKYGKIIGGLITSDGYHITAPKPTGEGAAQIAKQLVTQAGIDYSEIDYINGHGTGTQANDKM
EKNMYGKFFPTTTLISSTKGQTGHTLGAAGIIELINCLAAIEEQTVPATKNEIGIEGFPENFVYHQKREYPI
RNALNFSFAFGGNNSGVLLSSLDSPLETLPARENLKMAILSSVASISKNESLSITYEKVASNFNDFEALRFK
GARPPKTVNPAQFRKMDDFSKMVAVTTAQALIESNINLKKQDTSKVGIVFTTLSGPVEVVEGIEKQITTEGY
AHVSASRFPFTVMNAAAGMLSIIFKITGPLSVISTNSGALDGIQYAKEMMRNDNLDYVILVSANQWTDMSFM
WWQQLNYDSQMFVGSDYCSAQVLSRQALDNSPIILGSKQLKYSHKTFTDVMTIFDAALQNLLSDLGLTIKDI
KGFVWNERKKAVSSDYDFLANLSEYYNMPNLASGQFGFSSNGAGEELDYTVNESIEKGYYLVLSYSIFGGIS
FAIIEKR

GBS 404

Nucleotide and amino acid sequences of GBS 404 sequenced from serotype V isolated strain 2603 V/R are set forth in Ref. 3 as SEQ ID 8799 and SEQ ID 8800. These sequences are set forth below as SEQ ID NOS 46 and 47:

SEQ ID NO. 46

ATGAAAATAGATGACCTAAGAAAAAGCGACAATGTTGAAGATCGTCGCTCCAGTAGCGGAGGTTCATTCTCT
AGCGGAGGAAGTGGATTACCGATTCTTCAACTTTTATTGCTGCGAGGGAGTTGGAAAACCAAGCTTGTGGTT
TTAATCATCTTACTGCTACTTGGCGGAGGGGGACTAACCAGCATTTTTAATGACTCATCCTCACCTTCTAGT
TACCAATCTCAGAATGTCTCACGTTCTGTTGATAATAGCGCAACGAGAGAACAAATCGATTTCGTTAATAAA
GTCCTTGGCTCAACTGAGGATTTCTGGTCACAAGAATTCCAAACCCAAGGTTTTGGAAATTATAAGGAACCA
AAACTTGTTCTTTACACCAATTCAATTCAAACAGGTTGTGGTATAGGTGAATCTGCTTCAGGACCATTTTAT
TGTTCAGCAGATAAAAAAATCTATCTTGATATTTCTTTTTACAATGAATTATCACATAAATATGGTGCTACT
GGTGATTTTGCTATGGCCTACGTCATCGCCCACGAAGTTGGTCACCACATTCAAACAGAGTTAGGCATTATG
GATAAGTATAATAGAATGCGACACGGACTTACTAAGAAAGAAGCAAATGCTTTAAATGTTCGGCTAGAACTT
CAAGCAGATTATTATGCAGGGGTATGGGCTCACTACATCAGGGGAAAAAATCTCTTAGAACAAGGAGACTTT
GAAGAGGCCATGAATGCTGCCCACGCCGTCGGAGACGATACCCTTCAGAAAGAAACCTACGGAAAATTAGTG
CCTGATAGCTTTACCCATGGAACAGCTGAACAACGCCAACGTTGGTTTAACAAAGGCTTTCAATATGGTGAC
ATCCAACACGGTGATACTTTCTCCGTAGAACATCTA

SEQ ID NO. 47

MKIDDLRKSDNVEDRRSSSGGSFSSGGSGLPILQLLLLRGSWKTKLVVLIILLLGGGGLTSIFNDSSSPSS
YQSQNVSRSVDNSATREQIDFVNKVLGSTEDFWSQEFQTQGFGNYKEPKLVLYTNSIQTGCGIGESASGPFY
CSADKKIYLDISFYNELSHKYGATGDFAMAYVIAHEVGHHIQTELGIMDKYNRMRHGLTKKEANALNVRLEL
QADYYAGVWAHYIRGKNLLEQGDFEEAMNAAHAVGDDTLQKETYGKLVPDSFTHGTAEQRQRWFNKGFQYGD
IQHGDTFSVEHL

GBS 690

Nucleotide and amino acid sequences of GBS 690 sequenced from serotype V isolated strain 2603 V/R are set forth in Ref. 3 as SEQ ID 9965 and SEQ ID 9966. These sequences are set forth as SEQ ID NOS 48 and 49 below:

SEQ ID NO. 48

ATGAGTAAACGACAAAATTTAGGAATTAGTAAAAAAGGAGCAATTATATCAGGGCTCTCAGTGGCACTAATT
GTAGTAATAGGTGGCTTTTATGGGTACAATCTCAACCTAATAAGAGTGCAGTAAAAACTAACTACAAAGTT
TTTAATGTTAGAGAAGGAAGTGTTTCGTCCTCAACTCTTTGACAGGAAAAGCTAAGGCTAATCAAGAACAG
TATGTGTATTTTGATGCTAATAAAGGTAATCGAGCAACTGTCACAGTTAAAGTGGGTGATAAAATCACAGCT
GGTCAGCAGTTAGTTCAATATGATACAACAACTGCACAAGCAGCCTACGACACTGCTAATCGTCAATTAAAT
AAAGTAGCGCGTCAGATTAATAATCTAAAGACAACAGGAAGTCTTCCAGCTATGGAATCAAGTGATCAATCT
TCTTCATCATCACAAGGACAAGGGACTCAATCGACTAGTGGTGCGACGAATCGTCTACAGCAAAATTATCAA
AGTCAAGCTAATGCTTCATACAACCAACAACTTCAAGATTTGAATGATGCTTATGCAGATGCACAGGCAGAA
GTAAATAAAGCACAAAAAGCATTGAATGATACTGTTATTACAAGTGACGTATCAGGGACAGTTGTTGAAGTT
AATAGTGATATTGATCCAGCTTCAAAAACTAGTCAAGTACTTGTCCATGTAGCAACTGAAGGTAAACTCCAA
GTACAAGGAACGATGAGTGAGTATGATTTGGCTAATGTTAAAAAAGACCAGGCTGTTAAAATAAAATCTAAG
GTCTATCCTGACAAGGAATGGGAAGGTAAAATTTCATATATCTCAAATTATCCAGAAGCAGAAGCAAACAAC
AATGACTCTAATAACGGCTCTAGTGCTGTAAATTATAAATATAAAGTAGATATTACTAGCCCTCTCGATGCA
TTAAAACAAGGTTTTACCGTATCAGTTGAAGTAGTTAATGGAGATAAGCACCTTATTGTCCCTACAAGTTCT
GTGATAAACAAAGATAATAAACACTTTGTTTGGGTATACAATGATTCTAATCGTAAAATTTCCAAAGTTGAA
GTCAAAATTGGTAAAGCTGATGCTAAGACACAAGAAATTTTATCAGGTTTGAAAGCAGGACAAATCGTGGTT
ACTAATCCAAGTAAAACCTTCAAGGATGGGCAAAAAATTGATAATATTGAATCAATCGATCTTAACTCTAAT
AAGAAATCAGAGGTGAAA

SEQ ID NO. 49
MSKRQNLGISKKGAIISGLSVALIVVIGGPLWVQSQPNKSAVKTNYKVFNVREGSVSSSTLLTGKAKANQEQ
YVYFDANKGNRATVTVKVGDKITAGQQLVQYDTTTAQAAYDTANRQLNKVARQINNLKTTGSLPAMESSDQS
SSSSQGQGTQSTSGATNRLQQNYQSQANASYNQQLQDLNDAYADAQAEVNKAQKALNDTVITSDVSGTVVEV
NSDIDPASKTSQVLVHVATEGKLQVQGTMSEYDLANVKKDQAVKIKSKVYPDKEWEGKISYISNYPEAEANN
NDSNNGSSAVNYKYKVDITSPLDALKQGFTVSVEVVNGDKHLIVPTSSVINKDNKHFVWVYNDSNRKISKVE
VKIGKADAKTQEILSGLKAGQIVVTNPSKTFKDGQKIDNIESIDLNSNKKSEVK

GBS 690 contains an N-terminal leader or signal sequence region which is indicated by the underlined sequence at the beginning of SEQ ID NO: 49 above. In one embodiment, one or more amino acids from the leader or signal sequence region of GBS 690 are removed. An example of such a GBS 690 fragment is set forth below as SEQ ID NO: 50.

SEQ ID NO: 50
FLWVQSQPNKSAVKTNYKVFNVREGSVSSSTLLTGKAKANQEQYVYFDANKGNRATVTVKVGDKITAGQQLV
QYDTTTAQAAYDTANRQLNKVARQINNLKTTGSLPAMESSDQSSSSSQGQGTQSTSGATNRLQQNYQSQANA
SYNQQLQDLNDAYADAQAEVNKAQKALNDTVITSDVSGTVVEVNSDIDPASKTSQVLVHVATEGKLQVQGTM
SEYDLANVKKDQAVKIKSKVYPDKEWEGKISYISNYPEAEANNNDSNNGSSAVNYKYKVDITSPLDALKQGF
TVSVEVVNGDKHLIVPTSSVINKDNKHFVWVYNDSNRKISKVEVKIGKADAKTQEILSGLKAGQIVVTNPSK
TFKDGQKIDNIESIDLNSNKKSEVK

GBS 691

GBS 691 refers to an iron compound ABC transporter, or a substrate binding protein. Nucleotide and amino acid sequences of GBS 691 sequenced from serotype V isolated strain 2603 V/R are set forth in Ref. 3 as SEQ ID 3691 and SEQ ID 3692. These sequences are set forth as SEQ ID NOS 51 and 52 below:

SEQ ID NO. 51
ATGAAAAAAATTGGAATTATTGTCCTCACACTACTGACCTTCTTTTTGGTATCTTGCGGACAACAAACTAAA
CAAGAAAGCACTAAAACAACTATTTCTAAAATGCCTAAAATTGAAGGCTTCACCTATTATGGAAAAATTCCT
GAAAATCCGAAAAAAGTAATTAATTTTACATATTCTTACACTGGGTATTTATTAAAACTAGGTGTTAATGTT
TCAAGTTACAGTTTAGACTTAGAAAAAGATAGCCCCGTTTTTGGTAAACAACTGAAAGAAGCTAAAAAATTA
ACTGCTGATGATACAGAAGCTATTGCCGCACAAAAACCTGATTTAATCATGGTTTTCGATCAAGATCCAAAC
ATCAATACTCTGAAAAAAATTGCACCAACTTTAGTTATTAAATATGGTGCACAAAATTATTTAGATATGATG
CCAGCCTTGGGGAAAGTATTCGGTAAAGAAAAAGAAGCTAATCAGTGGGTTAGCCAATGGAAAACTAAAACT
CTCGCTGTCAAAAAAGATTTACACCATATCTTAAAGCCTAACACTACTTTTACTATTATGGATTTTTATGAT
AAAAATATCTATTTATATGGTAATAATTTTGGACGCGGTGGAGAACTAATCTATGATTCACTAGGTTATGCT
GCCCCAGAAAAAGTCAAAAAAGATGTCTTTAAAAAAGGGTGGTTTACCGTTTCGCAAGAAGCAATCGGTGAT
TACGTTGGAGATTATGCCCTTGTTAATATAAACAAAACGACTAAAAAAGCAGCTTCATCACTTAAAGAAAGT
GATGTCTGGAAGAATTTACCAGCTGTCAAAAAAGGCACATCATAGAAAGTAACTACGACGTGTTTATTTC
TCTGACCCTCTATCTTTAGAAGCTCAATTAAAATCATTTACAAAGGCTATCAAAGAAAATACAAAT

SEQ ID NO. 52
MKKIGIIVLTLLTFFLVSCGQQTKQESTKTTISKMPKIEGPTYYGKIPENPKKVINFTYSYTGYLLKLGVNV
SSYSLDLEKDSPVFGKQLKEAKKLTADDTEAIAAQKPDLIMVFDQDPNINTLKKIAPTLVIKYGAQNYLDMM
PALGKVPGKEKEANQWVSQWKTKTLAVKKDLHHILKPNTTPTIMDPYDKNIYLYGNNFGRGGELIYDSLGYA
APEKVKKDVFKKGWFTVSQEAIGDYVGDYALVNINKTTKKAASSLKESDVWKNLPAVKKGHIIESNYDVFYF
SDPLSLEAQLKSPTKAIKENTN

GBS 691 contains an N-terminal leader or signal sequence region which is indicated by the underlined sequence at the beginning of SEQ ID NO: 52 above. In one embodiment, one or more amino

acids are removed from the leader or signal sequence region of GBS 691. An example of such a GBS 691 fragment is set forth below as SEQ ID NO: 53.

SEQ ID NO: 53
EGFTYYGKIPENPKKVINFTYSYTGYLLKLGVNVSSYSLDLEKDSPVFGKQLKEAKKLTADDTEAIAAQKPD
LIMVFDQDPNINTLKKIAPTLVIKYGAQNYLDMMPALGKVFGKEKEANQWVSQWKTKTLAVKKDLHHILKPN
TTFTIMDFYDKNIYLYGNNFGRGGELIYDSLGYAAPEKVKKDVFKKGWFTVSQEAIGDYVGDYALVNINKTT
KKAASSLKESDVWKNLPAVKKGHIIESNYDVFYFSDPLSLEAQLKSFTKAIKENTN

GBS 691 contains a C-terminal transmembrane or cytosplasmic region which is indicated by the underlined sequence at the end of SEQ ID NO: 52 above. In one embodiment, one or more amino acids are removed from the transmembrane or cytoplasmic region of GBS 691. An example of such a GBS 691 fragment is set forth below as SEQ ID NO: 54.

SEQ ID NO: 54
MKKIGIIVLTLLTFFLVSCGQQTKQESTKTTISKMPKIEGFTYYGKIPENPKKVINFTYSYTGYLLKLGVNV
SSYSLDLEKDSPVFGKQLKEAKKLTADDTEAIAAQKPDLIMVFDQDPNINTLKKIAPTLVIKYGAQNYLDMM
PALGKVFGKEKEANQWVSQWKTKTLAVKKDLHHILKPNTTFTIMDFYDKNIYLYGNNFGRGGELIYDSLGYA
APEKVKKDVFKKGWFTVSQEAIGDYVGDYALVNINKTTKKAASSLKESDVWKNLPAVKKGHIIESNYDVFYF
SDPLSLEAQLKSFT

In one embodiment, one or more amino acids from the leader or signal sequence region and one or more amino acids from the transmembrane or cytosplasmic region are removed from GBS 691. One example of such a GBS 691 fragment is set forth below as SEQ ID NO: 55

SEQ ID NO: 55
EGFTYYGKIPENPKKVINFTYSYTGYLLKLGVNVSSYSLDLEKDSPVFGKQLKEAKKLTADDTEAIAAQKPD
LIMVFDQDPNINTLKKIAPTLVIKYGAQNYLDMMPALGKVFGKEKEANQWVSQWKTKTLAVKKDLHHILKPN
TTFTIMDFYDKNIYLYGNNFGRGGELIYDSLGYAAPEKVKKDVFKKGWFTVSQEAIGDYVGDYALVNINKTT
KKAASSLKESDVWKNLPAVKKGHIIESNYDVFYFSDPLSLEAQLKSFT

Additional examples of GBS antigens which may be used in combination with GBS 80 are set forth below.

GBS 4

GBS 4 refers to another putative cell wall surface anchor family protein. Nucleotide and amino acid sequences of GBS 4 sequenced from serotype V isolated strain 2603 V/R are set forth in Ref. 3 as SEQ ID 1 and SEQ ID 2. These sequences are also set forth below as SEQ ID NOS 56 and 57:

SEQ ID NO. 56
ATGAAAGTGAAAAATAAGATTTTAACGATGGTAGCACTTACTGTCTTAACATGTGCTACTTATTCATCAATC
GGTTATGCTGATACAAGTGATAAGAATACTGACACGAGTGTCGTGACTACGACCTTATCTGAGGAGAAAAGA
TCAGATGAACTAGACCAGTCTAGTACTGGTTCTTCTTCTGAAAATGAATCGAGTTCATCAAGTGAACCAGAA
ACAAATCCGTCAACTAATCCACCTACAACAGAACCATCGCAACCCTCACCTAGTGAAGAGAACAAGCCTGAT
GGTAGAACGAAGACAGAAATTGGCAATAATAAGGATATTTCTAGTGGAACAAAAGTATTAATTTCAGAAGAT
AGTATTAAGAATTTTAGTAAAGCAAGTAGTGATCAAGAAGAAGTGGATCGCGATGAATCATCATCTTCAAAA
GCAAATGATGGGAAAAAAGGCCACAGTAAGCCTAAAAAGGAACTTCCTAAAACAGGAGATAGCCACTCAGAT
ACTGTAATAGCATCTACGGGAGGGATTATTCTGTTATCATTAAGTTTTTACAATAAGAAAATGAAACTTTAT

SEQ ID NO. 57
MKVKNKILTMVALTVLTCATYSSIGYADTSDKNTDTSVVTTTLSEEKRSDELDQSSTGSSSENESSSSSEPE
TNPSTNPPTTEPSQPSPSEENKPDGRTKTEIGNNKDISSGTKVLISEDSIKNFSKASSDQEEVDRDESSSSK
ANDGKKGHSKPKKELPKTGDSHSDTVIASTGGIILLSLSFYNKKMKLY

GBS 4 contains an N-terminal leader or signal sequence which is underlined at the beginning of SEQ ID NO: 57 above. In one embodiment, one or more amino acids from the N-terminal leader or signal peptide domain of GBS 4 are removed. An example of such a GBS 4 fragment is set forth below as SEQ ID NO 58.

SEQ ID NO 58
DTSDKNTDTSVVTTTLSEEKRSDELDQSSTGSSSENESSSSSEPETNPSTNPPTTEPSQPSPSEENKPDGRT
KTEIGNNKDISSGTKVLISEDSIKNFSKASSDQEEVDRDESSSSKANDGKKGHSKPKKELPKTGDSHSDTVI
ASTGGIILLSLSFYNKKMKLY

A further N-terminal section of GBS 4 may be removed to facilitate recombinant expression. An example of such a GBS 4 fragment is set forth below as SEQ ID NO: 59.

SEQ ID NO: 59
DQSSTGSSSENESSSSSEPETNPSTNPPTTEPSQPSPSEENKPDGRTKTEIGNNKDISSGTKVLISEDSIKN
FSKASSDQEEVDRDESSSSKANDGKKGHSKPKKELPKTGDSHSDTVIASTGGIILLSLSFYNKKMKLY

GBS 4 contains an C-terminal transmembrane region which is underlined at the end of SEQ ID NO: 57 above. In one embodiment, one or more amino acids from the C-terminal transmembrane region is removed. An example of such a GBS 4 fragment is set forth below as SEQ ID NO: 60.

SEQ ID NO: 60
MKVKNKILTMVALTVLTCATYSSIGYADTSDKNTDTSVVTTTLSEEKRSDELDQSSTGSSSENESSSSSEPE
TNPSTNPPTTEPSQPSPSEENKPDGRTKTEIGNNKDISSGTKVLISEDSIKNFSKASSDQEEVDRDESSSSK
ANDGKKGHSKPKKE

In one embodiment, both the N-terminal leader or signal domain and the C-terminal transmembrane domain are removed from the GBS 4 sequence. An example of such a GBS 4 fragment is set forth below as SEQ ID NO: 61.

SEQ ID NO: 61
DTSDKNTDTSVVTTTLSEEKRSDELDQSSTGSSSENESSSSSEPETNPSTNPPTTEPSQPSPSEENKPDGRT
KTEIGNNKDISSGTKVLISEDSIKNFSKASSDQEEVDRDESSSSKANDGKKGHSKPKKE

In yet another embodiment, the N-terminal leader or signal domain, a further N-terminal region and the C-terminal transmembrane domain are removed from the GBS 4 sequence. An example of such a GBS 4 fragment is set forth below as SEQ ID NO: 62.

SEQ ID NO: 62
DQSSTGSSSENESSSSSEPETNPSTNPPTTEPSQPSPSEENKPDGRTKTEIGNNKDISSGTKVLISEDSIKN
FSKASSDQEEVDRDESSSSKANDGKKGHSKPKKE

GBS 22

GBS 22 refers to a putative adhesion lipoprotein. Nucleotide and amino acid sequences of GBS 22 sequenced from serotype V isolated strain 2603 V/R are set forth in Ref. 3 as SEQ 8583 and SEQ ID 8584. These sequences are set forth below as SEQ ID NOS 63 and 64:

SEQ ID NO. 63
ATGAAAAGGATACGAAAAGCCTTATTTTTGTTCTCGGAGTAGTTACCCTAATTTGCTTATGTGCTTGTACT
AAACAAAGCCAGCAAAAAAATGGCTTGTCAGTAGTGACTAGCTTTTATCCAGTATATTCCATTACAAAAGCA

GTTTCTGGTGATTTGAATGATATTAAAATGATTCGATCACAGTCAGGTATTCATGGTTTTGAACCCTCATCA
AGTGATGTTGCTGCCATTTATGATGCTGATCTATTTCTTTATCATTCGCACACACTAGAAGCTTGGGCGAGA
CGTTTGGAACCTAGTTTGCATCACTCTAAAGTATCTGTAATTGAAGCTTCAAAAGGTATGACTTTGGATAAA
GTTCATGGCTTAGAAGATGTAGAGGCAGAAAAAGGAGTAGATGAGTCAACCTTGTATGACCCTCACACTTGG
AATGACCCTGTAAAAGTATCTGAGGAAGCACAACTCATCGCTACACAATTAGCTAAAAAGGATCCTAAAAAC
GCTAAGGTTTATCAAAAAAATGCTGATCAATTTAGTGACAAGGCAATGGCTATTGCAGAGAAGTATAAGCCA
AAATTTAAAGCTGCAAAGTCTAAATACTTTGTGACTTCACATACAGCATTCTCATACTTAGCTAAGCGATAC
GGATTGACTCAGTTAGGTATTGCAGGTGTCTCAACCGAGCAAGAACCTAGTGCTAAAAAATTAGCCGAAATT
CAGGAGTTTGTGAAAACATATAAGGTTAAGACTATTTTTGTTGAAGAAGGAGTCTCACCTAAATTAGCTCAA
GCAGTAGCTTCAGCTACTCGAGTTAAAATTGCAAGTTTAAGTCCTTTARAAGCAGTTCCCAAAAACAATAAA
GATTACTTAGAAAATTTGGAAACTAATCTTAAGGTACTTGTCAAATCGTTAAATCAATAG

SEQ ID NO. 64

MKRIRKSLIFVLGVVTLICLCACTKQSQQKNGLSVVTSFYPVYSITKAVSGDLNDIKMIRSQSGIHGFEPSS
SDVAAIYDADLFLYHSHTLEAWARRLEPSLHHSKVSVIEASKGMTLDKVHGLEDVEAEKGVDESTLYDPHTW
NDPVKVSEEAQLIATQLAKKDPKNAKVYQKNADQFSDKAMAIAEKYKPKFKAAKSKYFVTSHTAFSYLAKRY
GLTQLGIAGVSTEQEPSAKKLAEIQEFVKTYKVKTIFVEEGVSPKLAQAVASATRVKIASLSPLXAVPKNNK
DYLENLETNLKVLVKSLNQ

GBS 85

GBS 85 refers to a putative cell division protein (DivIB). Nucleotide and amino acid sequences of GBS 85 sequenced from serotype V isolated strain 2603 V/R are set forth in Ref. 3 as SEQ ID 215 and SEQ ID 216. These sequences are set forth below as SEQ ID NOS 65 and 66:

SEQ ID NO. 65

ATGCCTAAGAAGAAATCAGATACCCCAGAAAAAGAAGAAGTTGTCTTAACGGAATGGCAAAAGCGTAACCTT
GAATTTTTAAAAAAACGCAAAGAAGATGAAGAAGAACAAAAACGTATTAACGAAAAATTACGCTTAGATAAA
AGAAGTAAATTAAATATTTCTTCTCCTGAAGAACCTCAAAATACTACTAAAATTAAGAAGCTTCATTTTCCA
AAGATTTCAAGACCTAAGATTGAAAAGAAACAGAAAAAAGAAAAAATAGTCAACAGCTTAGCCAAAACTAAT
CGCATTAGAACTGCACCTATATTTGTAGTAGCATTCCTAGTCATTTTAGTTTCCGTTTTCCTACTAACTCCT
TTTAGTAAGCAAAAAACAATAACAGTTAGTGGAAATCAGCATACACCTGATGATATTTTGATAGAGAAAACG
AATATTCAAAAAAACGATTATTTCTTTTCTTTAATTTTTAAACATAAAGCTATTGAACAACGTTTAGCTGCA
GAAGATGTATGGGTAAAAACAGCTCAGATGACTTATCAATTTCCCAATAAGTTTCATATTCAAGTTCAAGAA
AATAAGATTATTGCATATGCACATACAAAGCAAGGATATCAACCTGTCTTGGAAACTGGAAAAAAGGCTGAT
CCTGTAAATAGTTCAGAGCTACCAAAGCACTTCTTAACAATTAACCTTGATAAGGAAGATAGTATTAAGCTA
TTAATTAAAGATTTAAAGGCTTTAGACCCTGATTTAATAAGTGAGATTCAGGTGATAAGTTTAGCTGATTCT
AAAACGACACCTGACCTCCTGCTGTTAGATATGCACGATGGAAATAGTATTAGAATACCATTATCTAAATTT
AAAGAAAGACTTCCTTTTTACAAACAAATTAAGAAGAACCTTAAGGAACCTTCTATTGTTGATATGGAAGTG
GGAGTTTACACAACAACAAATACCATTGAATCAACCCCTGTTAAAGCAGAAGATACAAAAAATAAATCAACT
GATAAAACACAAACACAAAATGGTCAGGTTGCGGAAAATAGTCAAGGACAAACAAATAACTCAAATACTAAT
CAACAAGGACAACAGATAGCAACAGAGCAGGCACCTAACCCTCAAAATGTTAAT

SEQ ID NO. 66

MPKKKSDTPEKEEVVLTEWQKRNLEFLKKRKEDEEEQKRINEKLRLDKRSKLNISSPEEPQNTTKIKKLHFP
KISRPKIEKKQKKEKIVNSLAKTNRIRTAPIFVVAFLVILVSVFLLTPFSKQKTITVSGNQHTPDDILIEKT
NIQKNDYFFSLIFKHKAIEQRLAAEDVWVKTAQMTYQPPNKFHIQVQENKIIAYAHTKQGYQPVLETGKKAD
PVNSSELPKHFLTINLDKEDSIKLLIKDLKALDPDLISEIQVISLADSKTTPDLLLLDMHDGNSIRIPLSKF
KERLPFYKQIKKNLKEPSIVDMEVGVYTTNTIESTPVKAEDTKNKSTDKTQTQNGQVAENSQGQTNNSNTN
QQGQQIATEQAPNPQNVN

GBS 147

GBS 147 refers to a putative protease. Nucleotide and amino acid sequences of GBS 147 sequenced from serotype V isolated strain 2603 V/R are set forth in Ref. 3 as SEQ ID 8525 and SEQ ID 8526. These sequences are set forth below as SEQ ID NOS 67 and 68.

SEQ ID NO. 67

GTGGATAAACATCACTCAAAAAAGGCTATTTTAAAGTTAACACTTATAACAACTAGTATTTTATTAATGCAT
AGCAATCAAGTGAATGCAGAGGAGCAAGAATTAAAAAACCAAGAGCAATCACCTGTAATTGCTAATGTTGCT
CAACAGCCATCGCCATCGGTAACTACTAATACTGTTGAAAAAACATCTGTAACAGCTGCTTCTGCTAGTAAT
ACAGCGAAAGAAATGGGTGATACATCTGTAAAAAATGACAAAACAGAAGATGAATTATTAGAAGAGTTATCT
AAAAACCTTGATACGTCTAATTTGGGGGCTGATCTTGAAGAAGAATATCCCTCTAAACCAGAGACAACCAAC
AATAAAGAAAGCAATGTAGTAACAAATGCTTCAACTGCAATAGCACAGAAAGTTCCCTCAGCATATGAAGAG
GTGAAGCCAGAAAGCAAGTCATCGCTTGCTGTTCTTGATACATCTAAAATAACAAAATTACAAGCCATAACC
CAAAGAGGAAAGGAAATGTAGTAGCTATTATTGATACTGGCTTTGATATTAACCATGATATTTTTCGTTTA
GATAGCCCAAAAGATGATAAGCACAGCTTTAAAACTAAGACAGAATTTGAGGAATTAAAAGCAAAACATAAT
ATCACTTATGGGAAATGGGTTAACGATAAGATTGTTTTTGCACATAACTACGCCAACAATACAGAAACGGTG
GCTGATATTGCAGCAGCTATGAAAGATGGTTATGGTTCAGAAGCAAAGAATATTTCGCATGGTACACACGTT
GCTGGTATTTTTGTAGGTAATAGTAAACGTCCAGCAATCAATGGTCTTCTTTTAGAAGGTGCAGCGCCAAAT
GCTCAAGTCTTATTAATGTCGTATTCCAGATAAAATTGATTCGGACAAATTTGGTGAAGCATATGCTAAAGCA
ATCACAGACGCTGTTAATCTAGGAGCAAAAACGATTAATATGAGTATTGGAAAAACAGCTGATTCTTTAATT
GCTCTCAATGATAAAGTTAAATTAGCACTTAAATTAGCTTCTGAGAAGGGCGTTGCAGTTGTTGTGGCTGCC
GGAAATGAAGGCGCATTTGGTATGGATTATAGCAAACCATTATCAACTAATCCTGACTACGGTACGGTTAAT
AGTCCAGCTATTTCTGAAGATACTTTGAGTGTTGCTAGCTATGAATCACTTAAAACTATCAGTGAGGTCGTT
GAAACAACTATTGAAGGTAAGTTAGTTAAGTTGCCGATTGTGACTTCTAAACCTTTTGACAAAGGTAAGGCC
TACGATGTGGTTTATGCCAATTATGGTGCAAAAAAAGACTTTGAAGGTAAGGACTTAAAAGTAAGATTGCA
TTAATTGAGCGTGGTGGTGGACTTGATTTTATGACTAAAATCACTCATGCTACAAATGCAGGTGTTGTTGGT
ATCGTTATTTTTAACGATCAAGAAAAACGTGGAAATTTTCTAATTCCTTACCGTGAATTACCTGTGGGGATT
ATTAGTAAAGTAGATGGCGAGCGTATAAAAAATACTTCAAGTCAGTTAACATTTAACCAGAGTTTTGAAGTA
GTTGATAGCCAAGGTGGTAATCGTATGCTGGAACAATCAAGTTGGGGCGTGACAGCTGAAGGAGCAATCAAG
CCTGATGTAACAGCTTCTGGCTTTGAAATTTATTCTTCAACCTATAATAATCAATACCCAAACAATGTCTGGT
ACAAGTATGGCTTCACCACATGTTGCAGGATTAATGACAATGCTTCAAAGTCATTTGGCTGAGAAATATAAA
GGGATGAATTTAGATTCTAAAAAATTGCTAGAATTGTCTAAAAACATCCTCATGAGCTCAGCAACAGCATTA
TATAGTGAAGAGGATAAGGCGTTTTATTCACCACGTCAGCAAGGTGCAGGTGTAGTTGATGCTGAAAAAGCT
ATCCAAGCTCAATATTATATTACTGGAAACGATGGCAAAGCTAAAATTAATCTCAAACGAATGGGAGATAAA
TTTGATATCACAGTTACAATTCATAAACTTGTAGAAGGTGTCAAAGAATTGTATTATCAAGCTAATGTAGCA
ACAGAACAAGTAAATAAAGGTAAATTTGCCCTTAAACCACAAGCCTTGCTAGATACTAATTGGCAGAAAGTA
ATTCTTCGTGATAAAGAAACACAAGTTCGATTTACTATTGATGCTAGTCAATTTAGTCAGAAATTAAAAGAA
CAGATGGCAAATGGTTATTTCTTAGAAGGTTTTGTACGTTTTAAAGAAGCCAAGGATAGTAATCAGGAGTTA
ATGAGTATTCCTTTTGTAGGATTTAATGGTGATTTTGCGAACTTACAAGCACTTGAAACACCGATTTTATAAG
ACGCTTTCTAAAGGTAGTTTCTACTATAAACCAAATGATACAACTCATAAAGACCAATTGGAGTACAATGAA
TCAGCTCCTTTTGAAAGCAACAACTATACTGCCTTGTTAACACAATCAGCGTCTTGGGGCTATGTTGATTAT
GTCAAAAATGGTGGGGAGTTAGAATTAGCACCGGAGAGTCCAAAAAGAATTATTTTAGGAACTTTTGAGAAT
AAGGTTGAGGATAAAACAATTCATCTTTTGGAAAGAGATGCAGCGAATAATCCATATTTTGCCATTTCTCCA
AATAAAGATGGAAATAGGGACGAAATCACTCCCCAGGCAACTTTCTTAAGAAATGTTAAGGATATTTCTGCT
CAAGTTCTAGATCAAAATGGAAATGTTATTTGGCAAAGTAAGGTTTTACCATCTTATCGTAAAAATTTCCAT
AATAATCCAAAGCAAAGTGATGGTCATTATCGTATGGATGCTCTTCAGTGGAGTGGTTTAGATAAGGATGGC
AAAGTTGTAGCAGATGGTTTTTATACTTATCGCTTACGTTACACACCAGTAGCAGAAGGAGCAAATAGTCAG
GAGTCAGACTTTAAAGTACAAGTAAGTACTAAGTCACCAAATCTTCCTTCACGAGCTCAGTTTGATGAAACT
AATCGAACATTAAGCTTAGCCATGCCTAAGGAAAGTAGTTATGTTCCTACATATCGTTTACAATTAGTTTTA
TCTCATGTTGTAAAAGATGAAGAATATGGGGATGAGACTTCTTACCATTATTTCCATATAGATCAAGAAGGT
AAAGTGACACTTCCTAAAACGGTTAAGATAGGAGAGAGTGAGGTTGCGGTAGACCCTAAGGCCTTGACACTT
GTTGTGGAAGATAAAGCTGGTAATTTCGCAACGGTAAAATTGTCTGATCTCTTGAATAAGGCAGTAGTATCA
GAGAAAGAAAACGCTATAGTAATTTCTAACAGTTTCAAATATTTTGATAACTTGAAAAAAGAACCTATGTTT
ATTTCTAAAAAAGAAAAGTAGTAAACAAGAATCTAGAAGAAATAATATTAGTTAAGCCGCAAACTACAGTT
ACTACTCAATCATTGTCTAAAGAAATAACTAAATCAGGAAATGAGAAAGTCCTCACTTCTACAAACAATAAT

AGTAGCAGAGTAGCTAAGATCATATCACCTAAACATAACGGGGATTCTGTTAACCATACCTTACCTAGTACA
TCAGATAGAGCAACGAATGGTCTATTTGTTGGTACTTTGGCATTGTTATCTAGTTTACTTCTTTATTTGAAA
CCCAAAAAGACTAAAAATAATAGTAAA

SEQ ID NO. 68
VDKHHSKKAILKLTLITTSILLMHSNQVNAEEQELKNQEQSPVIANVAQQPSPSVTTNTVEKTSVTAASASN
TAKEMGDTSVKNDKTEDELLEELSKNLDTSNLGADLEEEYPSKPETTNNKESNVVTNASTAIAQKVPSAYEE
VKPESKSSLAVGLMTMLQSTKLQAITQRGKGNVVAIIDTGFDINHDIFRLDSPKDDKHSFKTKTEFEELKAKHN
ITYGKWVNDKIVFAHNYANNTETVADIAAAMKDGYGSEAKNISHGTHVAGIFVGNSKRPAINGLLLEGAAPN
AQVLLMRIPDKIDSDKFGEAYAKAITDAVNLGAKTINMSIGKTADSLIALNDKVKLALKLASEKGVAVVVAA
GNEGAFGMDYSKPLSTNPDYGTVNSPAISEDTLSVASYESLKTISEVVETTIEGKLVKLPIVTSKPFDKGKA
YDVVYANYGAKKDFEGKDFKGKIALIERGGGLDFMTKITHATNAGVVGIVIFNDQEKRGNFLIPYRELPVGI
ISKVDGERIKNTSSQLTFNQSFEVVDSQGGNRMLEQSSWGVTAEGAIKPDVTASGFEIYSSTYNNQYQTMSG
TSMASPHVAGLMTMLQSHLAEKYKGMNLDSKKLLELSKNILMSSATALYSEEDKAFYSPRQQGAGVVDAEKA
IQAQYYITGNDGKAKINLKRMGDKFDITVTIHKLVEGVKELYYQANVATEQVNKGKFALKPQALLDTNWQKV
ILRDKETQVRFTIDASQFSQKLKEQMANGYFLEGFVRFKEAKDSNQELMSIPFVGFNGDFANLQALETPIYK
TLSKGSFYYKPNDTTHKDQLEYNESAPFESNNYTALLTQSASWGYVDYVKNGGELELAPESPKRIILGTFEN
KVEDKTIHLLERDAANNPYFAISPNKDGNRDEITPQATFLRNVKDISAQVLDQNGNVIWQSKVLPSYRKNFH
NNPKQSDGHYRMDALQWSGLDKDGKVVADGFYTYRLRYTPVAEGANSQESDFKVQVSTKSPNLPSRAQFDET
NRTLSLAMPKESSYVPTYRLQLVLSHVVKDEEYGDETSYHYFHIDQEGKVTLPKTVKIGESEVAVDPKALTL
VVEDKAGNFATVKLSDLLNKAVVSEKENAIVISNSFKYFDNLKKEPMFISKKEKVVNKNLEEIILVKPQTTV
TTQSLSKEITKSGNEKVLTSTNNNSSRVAKIISPKHNGDSVNHTLPSTSDRATNGLFVGTLALLSSLLLYLK
PKKTKNNSK

GBS 147 contains an N-terminal leader or signal sequence region which is indicated by the underlined sequence at the beginning of SEQ ID NO 68 above. In one embodiment, one or more amino acids from the leader or signal sequence region of GBS 147 are removed. An example of such a GBS 147 fragment is set forth below as SEQ ID NO: 69.

SEQ ID NO: 69
EEQELKNQEQSPVIANVAQQPSPSVTTNTVEKTSVTAASASNTAKEMGDTSVKNDKTEDELLEELSKNLDTS
NLGADLEEEYPSKPETTNNKESNVVTNASTAIAQKVPSAYEEVKPESKSSLAVLDTSKITKLQAITQRGKGN
VVAIIDTGFDINHDIFRLDSPKDDKHSFKTKTEFEELKAKHNITYGKWVNDKIVFAHNYANNTETVADIAAA
MKDGYGSEAKNISHGTHVAGIFVGNSKRPAINGLLLEGAANPAQVLLMRIPDKIDSDKFGEAYAKAITDAVN
LGAKTINMSIGKTADSLIALNDKVKLALKLASEKGVAVVVAAGNEGAFGMDYSKPLSTNPDYGTVNSPAISE
DTLSVASYESLKTISEVVETTIEGKLVKLPIVTSKPFDKGKAYDVVYANYGAKKDFEGKDFKGKIALIERGG
GLDFMTKITHATNAGVVGIVIFNDQEKRGNFLIPYRELPVGIISKVDGERIKNTSSQLTFNQSFEVVDSQGG
NRMLEQSSWGVTAEGAIKPDVTASGFEIYSSTYNNQYQTMSGTSMASPHVAGLMTMLQSHLAEKYKGMNLDS
KKLLELSKNILMSSATALYSEEDKAFYSPRQQGAGVVDAEKAIQAQYYITGNDGKAKINLKRMGDKFDITVT
IHKLVEGVKELYYQANVATEQVNKGKFALKPQALLDTNWQKVILRDKETQVRFTIDASQFSQKLKEQMANGY
FLEGFVRFKEAKDSNQELMSIPFVGFNGDFANLQALETPIYKTLSKGSFYYKPNDTTHKDQLEYNESAPFES
NNYTALLTQSASWGYVDYVKNGGELELAPESPKRIILGTFENKVEDKTIHLLERDAANNPYFAISPNKDGNR
DEITPQATFLRNVKDISAQVLDQNGNVIWQSKVLPSYRKNFHNNPKQSDGHYRMDALQWSGLDKDGKVVADG
FYTYRLRYTPVAEGANSQESDFKVQVSTKSPNLPSRAQFDETNRTLSLAMPKESSYVPTYRLQLVLSHVVKD
EEYGDETSYHYFHIDQEGKVTLPKTVKIGESEVAVDPKALTLVVEDKAGNFATVKLSDLLNKAVVSEKENAI
VISNSFKYFDNLKKEPMFISKKEKVVNKNLEEIILVKPQTTVTTQSLSKEITKSGNEKVLTSTNNNSSRVAK
IISPKHNGDSVNHTLPSTSDRATNGLFVGTLALLSSLLLYLKPKKTKNNSK

GBS 147 also contains a C-terminal transmembrane and/or cytoplasmic region which may be located within the underlined sequence near the end of SEQ ID NO: 68 above. In one embodiment, one or more amino acids from the transmembrane and/or cytoplasmic region are removed. An example of such a GBS 147 fragment is set forth below as SEQ ID NO: 70.

SEQ ID NO: 70

VDKHHSKKAILKLTLITTSILLMHSNQVNAEEQELKNQEQSPVIANVAQQPSPSVTTNTVEKTSVTAASASN
TAKEMGDTSVKNDKTEDELLEELSKNLDTSNLGADLEEEYPSKPETTNNKESNVVTNASTAIAQKVPSAYEE
VKPESKSSLAVLDTSKITKLQAITQRGKGNVVAIIDTGFDINHDIFRLDSPKDDKHSFKTKTEFEELKAKHN
ITYGKWVNDKIVFAHNYANNTETVADIAAAMKDGYGSEAKNISHGTHVAGIFVGNSKRPAINGLLLEGAAPN
AQVLLMRIPDKIDSDKFGEAYAKAITDAVNLGAKTINMSIGKTADSLIALNDKVKLALKLASEKGVAVVVAA
GNEGAPGMDYSKPLSTNPDYGTVNSPAISEDTLSVASYESLKTISEVVETTIEGKLVKLPIVTSKPFDKGKA
YDVVYANYGAKKDFEGKDFKGKIALIERGGGLDFMTKITHATNAGVVGIVIFNDQEKRGNFLIPYRELPVGI
ISKVDGERIKNTSSQLTFNQSFEVVDSQGGNRMLEQSSWGVTAEGAIKPDVTASGFEIYSSTYNNQYQTMSG
TSMASPHVAGLMTMLQSHLAEKYKGMNLDSKKLLELSKNILMSSATALYSEEDKAFYSPRQQGAGVVDAEKA
IQAQYYITGNDGKAKINLKRMGDKFDITVTIHKLVEGVKELYYQANVATEQVNKGKFALKPQALLDTNWQKV
ILRDKETQVRFTIDASQFSQKLEQMANGYFLEGFVRPKEAKDSNQELMSIPFVGFNGDFANLQALETPIYK
TLSKGSFYYKPNDTTHKDQLEYNESAPFESNNYTALLTQSASWGYVDYVKNGGELELAPESPKRIILGTFEN
KVEDKTIHLLERDAANNPYFAISPNKDGNRDEITPQATFLRNVKDISAQVLDQNGNVIWQSKVLPSYRKNFH
NNPKQSDGHYRMDALQWSGLDKDGKVVADGFYTYRLRYTPVAEGANSQESDFKVQVSTKSPNLPSRAQFDET
NRTLSLAMPKESSYVPTYRLQLVLSHVVKDEEYGDETSYHYFHIDQEGKVTLPKTVKIGESEVAVDPKALTL
VVEDKAGNFATVKLSDLLNKAVVSEKENAIVISNSFKYFDNLKKEPMFISKKEKVVNKNLEEIILVKPQTTV
TTQSLSKEITKSGNEKVLTSTNNNSSRVAKIISPKHNGDSVNHT

In one embodiment, one or more amino acids from the leader or signal sequence region and one or more amino acids from the transmembrane or cytoplasmic region are removed from the GBS 147 sequence. An example of such a GBS 147 fragment is set forth below as SEQ ID NO 71.

SEQ ID NO: 71

EEQELKNQEQSPVIANVAQQPSPSVTTNTVEKTSVTAASASNTAKEMGDTSVKNDKTEDELLEELSKNLDTS
NLGADLEEEYPSKPETTNNKESNVVTNASTAIAQKVPSAYEEVKPESKSSLAVLDTSKITKLQAITQRGKGN
VVAIIDTGFDINHDIFRLDSPKDDKHSFKTKTEFEELKAKHNITYGKWVNDKIVFAHNYANNTETVADIAAA
MKDGYGSEAKNISHGTHVAGIFVGNSKRPAINGLLLEGAAPNAQVLLMRIPDKIDSDKFGEAYAKAITDAVN
LGAKTINMSIGKTADSLIALNDKVKLALKLASEKGVAVVVAAGNEGAFGMDYSKPLSTNPDYGTVNSPAISE
DTLSVASYESLKTISEVVETTIEGKLVKLPIVTSKPFDKGKAYDVVYANYGAKKDFEGKDFKGKIALIERGG
GLDFMTKITHATNAGVVGIVIFNDQEKRGNFLIPYRELPVGIISKVDGERIKNTSSQLTFNQSFEVVDSQGG
NRMLEQSSWGVTAEGAIKPDVTASGFEIYSSTYNNQYQTMSGTSMASPHVAGLMTMLQSHLAEKYKGMNLDS
KKLLELSKNILMSSATALYSEEDKAFYSPRQQGAGVVDAEKAIQAQYYITGNDGKAKINLKRMGDKFDITVT
IHKLVEGVKELYYQANVATEQVNKGKFALKPQALLDTNWQKVILRDKETQVRFTIDASQFSQKLEQMANGY
FLEGFVRPKEAKDSNQELMSIPFVGFNGDFANLQALETPIYKTLSKGSFYYKPNDTTHKDQLEYNESAPFES
NNYTALLTQSASWGYVDYVKNGGELELAPESPKRIILGTFENKVEDKTIHLLERDAANNPYFAISPNKDGNR
DEITPQATFLRNVKDISAQVLDQNGNVIWQSKVLPSYRKNFHNNPKQSDGHYRMDALQWSGLDKDGKVVADG
FYTYRLRYTPVAEGANSQESDFKVQVSTKSPNLPSRAQFDETNRTLSLAMPKESSYVPTYRLQLVLSHVVKD
EEYGDETSYHYFHIDQEGKVTLPKTVKIGESEVAVDPKALTLVVEDKAGNFATVKLSDLLNKAVVSEKENAI
VISNSFKYFDNLKKEPMFISKKEKVVNKNLEEIILVKPQTTVTTQSLSKEITKSGNEKVLTSTNNNSSRVAK
IISPKHNGDSVNHT

GBS 173

GBS 173 refers to an amidase family protein. Nucleotide and amino acid sequences of GBS 173 sequenced from serotype V isolated strain 2603 V/R are set forth in Ref. 3 as SEQ ID 8787 and SEQ ID 8788. These sequences are set forth below as SEQ ID NOS 72 and 73:

SEQ ID NO. 72

ATGAAACGTAAATACTTTATTCTTAATACGGTGACGGTTTTAACGTTAGCTGCTGCAATGAATACTAGCAGT
ATCTATGCTAATAGTACTGAGACAAGTGCTTCAGTAGTTCCTACTACAAATACTATCGTTCAAACTAATGAC
AGTAATCCTACCGCAAAATTTGTATCAGAATCAGGACAATCTGTAATAGGTCAAGTAAAACCAGATAATTCT
GCGGCGCTTACAACAGTTGACACGCCTCATCATATTTCAGCTCCAGATGCTTTAAAAACAACTCAATCAAGT
CCTGTCGTTGAGAGTACTTCTACTAAGTTAACTGAAGAGACTTACAAACAAAAAGATGGTCAAGATTTAGCC
AACATGGTGAGAAGTGGTCAAGTTACTAGTGAGGAACTCGTTAATATGGCATACGATATTATTGCTAAAGAA

AACCCATCTTTAAATGCAGTCATTACTACTAGACGCCAAGAAGCTATTGAAGAGGCTAGAAAACTTAAAGAT
ACCAATCAGCCGTTTTTAGGTGTTCCCTTGTTAGTCAAGGGGTTAGGGCACAGTATTAAAGGTGGTGAAACC
AATAATGGCTTGATCTATGCAGATGGAAAAATTAGCACATTTGACAGTAGCTATGTCAAAAAATATAAAGAT
TTAGGATTTATTATTTTAGGACAAACGAACTTTCCAGAGTATGGGTGGCGTAATATAACAGATTCTAAATTA
TACGGTCTAACGCATAATCCTTGGGATCTTGCTCATAATGCTGGTGGCTCTTCTGGTGGAAGTGCAGCAGCC
ATTGCTAGCGGAATGACGCCAATTGCTAGCGGTAGTGATGCTGGTGGTTCTATCCGTATTCCATCTTCTTGG
ACGGGCTTGGTAGGTTTAAAACCAACAAGAGGATTGGTGAGTAATGAAAAGCCAGATTCGTATAGTACAGCA
GTTCATTTTCCATTAACTAAGTCATCTAGAGACGCAGAAACATTATTAACTTATCTAAAGAAAAGCGATCAA
ACGCTAGTATCAGTTAATGATTTAAAATCTTTACCAATTGCTTATACTTTGAAATCACCAATGGGAACAGAA
GTTAGTCAAGATGCTAAAAACGCTATTATGGACAACGTCACATTCTTAAGAAAACAAGGATTCAAAGTAACA
GAGATAGACTTACCAATTGATGGTAGAGCATTAATGCGTGATTATTCAACCTTGGCTATTGGCATGGGAGGA
GCTTTTTCAACAATTGAAAAAGACTTAAAAAAACATGGTTTACTAAAGAAGACGTTGATCCTATTACTTGG
GCAGTTCATGTTATTTATCAAAATTCAGATAAGGCTGAACTTAAGAAATCTATTATGGAAGCCCAAAAACAT
ATGGATGATTATCGTAAGGCAATGGAGAAGCTTCACAAGCAATTTCCTATTTTCTTATCGCCAACGACCGCA
AGTTTAGCCCCTCTAAATACAGATCCCATATGTAACAGAGGAAGATAAAAGAGCGATTTATAATATGGAAAAC
TTGAGCCAAGAAGAAAGAATTGCTCTCTTTAATCGCCAGTGGGAGCCTATGTTGCGTAGAACACCTTTTACA
CAAATTGCTAATATGACAGGACTCCCAGCTATCAGTATCCCGACTTACTTATCTGAGTCTGGTTCTACCCATA
GGGACGATGTTAATGGCAGGTGCAAACTATGATATGGTATTAATTAAATTTGCAACTTTCTTTGAAAAACAT
CATGGTTTTAATGTTAAATGGCAAAGAATAATAGATAAAGAAGTGAAACCATCTACTGGCCTAATACAGCCT
ACTAACTCCCTCTTTAAAGCTCATTCATCATTAGTAAATTTAGAAGAAAATTCACAAGTTACTCAAGTATCT
ATCTCTAAAAAATGGATGAATCGTCTGTTAAAAATAAACCATCCGTAATGGCATATCAAAAAGCACTTCCT
AAAACAGGTGATACAGAATCAAGCCTATCTCCAGTTTTAGTAGTAACCCTTTTATTAGCTTGTTTTAGCTTT
GTAACAAAAAAGAATCAGAAAAGT

SEQ ID NO. 73

MKRKYFILNTVTVLTLAAAMNTSSIYANSTETSASVVPTTNTIVQTNDSNPTAKFVSESGQSVIGQVKPDNS
AALTTVDTPHHISAPDALKTTQSSPVVESTSTKLTEETYKQKDGQDLANMVRSGQVTSEELVNMAYDIIAKE
NPSLNAVITTRRQEAIEEARKLKDTNQPFLGVPLLVKGLGHSIKGGETNNGLIYADGKISTFDSSYVKKYKD
LGFIILGQTNFPEYGWRNITDSKLYGLTHNPWDLAHNAGGSSGGSAAAIASGMTPIASGSDAGGSIRIPSSW
TGLVGLKPTRGLVSNEKPDSYSTAVHFPLTKSSRDAETLLTYLKKSDQTLVSVNDLKSLPIAYTLKSPMGTE
VSQDAKNAIMDNVTFLRKQGFKVTEIDLPIDGRALMRDYSTLAIGMGGAPSTIEKDLKKHGFTKEDVDPITW
AVHVIYQNSDKAELKKSIMEAQKHMDDYRKAMEKLHKQFPIFLSPTTASLAPLNTDPVVTEEDKRAIYNMEN
LSQEERIALFNRQWEPMLRRTPFTQIANMTGLPAISIPTYLSESGLPIGTMLMAGANYDMVLIKFATFFEKH
HGFNVKWQRIIDKEVKPSTGLIQPTNSLFKAHSSLVNLEENSQVTQVSISKKWMKSSVKNKPSVMAYQKALP
KTGDTESSLSPVLVVTLLLACFSFVTKKNQKS

GBS 173 contains an N-terminal leader or signal sequence region which is indicated by the underlined sequences at the beginning of SEQ ID NO: 73 above. In one embodiment, one or more amino acids from the leader or signal sequence of GBS 173 are removed. An example of such a GBS 173 fragment is set forth below as SEQ ID NO: 74.

SEQ ID NO: 74

TTNTIVQTNDSNPTAKFVSESGQSVIGQVKPDNSAALTTVDTPHHISAPDALKTTQSSPVVESTSTKLTEET
YKQKDGQDLANMVRSGQVTSEELVNMAYDIIAKENPSLNAVITTRRQEAIEEARKLKDTNQPFLGVPLLVKG
LGHSIKGGETNNGLIYADGKISTFDSSYVKKYKDLGFIILGQTNFPEYGWRNITDSKLYGLTHNPWDLAHNA
GGSSGGSAAAIASGMTPIASGSDAGGSIRIPSSWTGLVGLKPTRGLVSNEKPDSYSTAVHFPLTKSSRDAET
LLTYLKKSDQTLVSVNDLKSLPIAYTLKSPMGTEVSQDAKNAIMDNVTFLRKQGFKVTEIDLPIDGRALMRD
YSTLAIGMGGAFSTIEKDLKKHGFTKEDVDPITWAVHVIYQNSDKAELKKSIMEAQKHMDDYRKAMEKLHKQ
FPIFLSPTTASLAPLNTDPYVTEEDKRAIYNMENLSQEERIALFNRQWEPMLRRTPFTQIANMTGLPAISIP
TYLSESGLPIGTMLMAGANYDMVLIKFATFFEKHHGFNVKWQRIIDKEVKPSTGLIQPTNSLFKAHSSLVNL
EENSQVTQVSISKKWMKSSVKNKPSVMAYQKALPKTGDTESSLSPVLVVTLLLACFSFVTKKNQKS

GBS 173 may also contain a C-terminal transmembrane and/or cytoplasmic region which may be located within the underlined region near the end of SEQ ID NO: 73 above. In one embodiment, one or

more amino acids from the transmembrane or cytoplasmic region of GBS 173 are removed. An example of such a GBS 173 fragment is set forth below as SEQ ID NO: 75.

SEQ ID NO: 75

MKRKYFILNTVTVLTLAAAMNTSSIYANSTETSASVVPTTNTIVQTNDSNPTAKFVSESGQSVIGQVKPDNS
AALTTVDTPHHISAPDALKTTQSSPVVESTSTKLTEETYKQKDGQDLANMVRSGQVTSEELVNMAYDIIAKE
NPSLNAVITTRRQEAIEEARKLKDTNQPFLGVPLLVKGLGHSIKGGETNNGLIYADGKISTFDSSYVKKYKD
LGFIILGQTNFPEYGWRNITDSKLYGLTHNPWDLAHNAGGSSGGSAAAIASGMTPIASGSDAGGSIRIPSSW
TGLVGLKPTRGLVSNEKPDSYSTAVHFPLTKSSRDAETLLTYLKKSDQTLVSVNDLKSLPIAYTLKSPMGTE
VSQDAKNAIMDNVTFLRKQGFKVTEIDLPIDGRALMRDYSTLAIGMGGAFSTIEKDLKKHGFTKEVDPITW
AVHVIYQNSDKAELKKSIMEAQKHMDDYRKAMEKLHKQFPIFLSPTTASLAPLNTDPYVTEEDKRAIYNMEN
LSQEERIALFNRQWEPMLRRTPFTQIANMTGLPAISIPTYLSESGLPIGTMLMAGANYDMVLIKFATFFEKH
HGFNVKWQRIIDKEVKPSTGLIQPTNSLFKAHSSLVNLEENSQVTQVSISKKWMKSSVKNK

In one embodiment, one or more amino acids from the leader or signal sequence region and one or more amino acids from the transmembrane or cytoplasmic region are removed. An example of such a GBS 173 fragment is set forth below as SEQ ID NO: 76.

SEQ ID NO: 76

TTNTIVQTNDSNPTAKFVSESGQSVIGQVKPDNSAALTTVDTPHHISAPDALKTTQSSPVVESTSTKLTEET
YKQKDGQDLANMVRSGQVTSEELVNMAYDIIAKENPSLNAVITTRRQEAIEEARKLKDTNQPFLGVPLLVKG
LGHSIKGGETNNGLIYADGKISTFDSSYVKKYKDLGFIILGQTNFPEYGWRNITDSKLYGLTHNPWDLAHNA
GGSSGGSAAAIASGMTPIASGSDAGGSIRIPSSWTGLVGLKPTRGLVSNEKPDSYSTAVHFPLTKSSRDAET
LLTYLKKSDQTLVSVNDLKSLPIAYTLKSPMGTEVSQDAKNAIMDNVTFLRKQGFKVTEIDLPIDGRALMRD
YSTLAIGMGGAFSTIEKDLKKHGFTKEDVDPITWAVHVIYQNSDKAELKKSIMEAQKHMDDYRKAMEKLHKQ
FPIFLSPTTASLAPLNTDPYVTEEDKRAIYNMENLSQEERIALFNRQWEPMLRRTPFTQIANMTGLPAISIP
TYLSESGLPIGTMLMAGANYDMVLIKFATFFEKHHGFNVKWQRIIDKEVKPSTGLIQPTNSLFKAHSSLVNL
EENSQVTQVSISKKWMKSSVKNK

GBS 313

Nucleotide and amino acid sequences of GBS 313 sequenced from serotype V isolated strain 2603 V/R are set forth in Ref. 3 as SEQ ID 4089 and SEQ ID 4090. These sequences are set forth as SEQ ID NOS 77 and 78 below:

SEQ ID NO. 77

ATGAAACGTATTGCTGTTTTAACTAGTGGTGGTGACGCCCCTGGTATGAACGCTGCTATCCGTGCAGTTGTT
CGTAAAGCAATTTCTGAAGGTATGGAAGTTTACGGCATCAACCAAGGTTACTATGGTATGGTGACAGGGGAT
ATTTTCCCTTTGGATGCTAATTCTGTTGGGGATACTATCAACCGTGGAGGAACGTTTTTACGTTCAGCACGT
TATCCTGAATTTGCTGAACTTGAAGGTCAGCTTAAAGGGATTGAACAGCTTAAAAAACAYCGGTATTGAAGGT
GTAGTAGTTATCGGTGGTGATGGTTCTTATCATGGTGCTATGCGTCTAACTGAGCACGGTTTCCCAGCTGTT
GGTTTGCCCGGTACAATTGATAACGATATCGTTGGCACTGACTATACTATTGGTTTTGACACAGCAGTTGCG
ACAGCAGTTGAGAATCTTGACCGTCTTCGTGATACATCAGCAAGTCATAACCGTACTTTTGTTGTTGAGGTT
ATGGGAAGAAATGCAGGAGATATCGCTCTTTGGTCAGGTATCGCTGCAGGTGCAGATCAAATTATTGTTCCT
GAAGAAGAGTTCAATATTGATGAAGTTGTCTCAAATGTTAGAGCTGGCTATGCAGCTGGTAAACATCACCAA
ATCATCGTCCTTGCAGAAGGTGTTATGAGTGGTGATGAGTTTGCAAAAACAATGAAAGCAGCAGGAGACGAT
AGCGATCTTCGTGTGACGAATTTAGGACATCTGCTCCGTGGTGGTAGTCCGACGGCTCGTGATCGTGTCTTA
GCATCTCGTATGGGAGCGTACGCTGTTCAATTGTTGAAAGAAGGTCGTGGTGGTTTAGCCGTTGGTGTCCAC
AACGAAGAAATGGTTGAAAGTCCAATTTTAGGTTTAGCAGAAGAAGGTGCTTTGTTCAGCTTGACTGATGAA
GGAAAAATCGTTGTTAATAATCCGCATAAAGCGGACCTTCGCTTGGCAGCACTTAATCGTGACCTTGCCAAC
CAAAGTAGTAAA

SEQ ID NO. 78

MKRIAVLTSGGDAPGMNAAIRAVVRKAISEGMEVYGINQGYYGMVTGDIFPLDANSVGDTINRGGTFLRSAR
YPEFAELEGQLKGIEQLKKHGIEGVVVIGGDGSYHGAMRLTEHGFPAVGLPGTIDNDIVGTDYTIGFDTAVA

TAVENLDRLRDTSASHNRTFVVEVMGRNAGDIALWSGIAAGADQIIVPEEEFNIDEVVSNVRAGYAAGKHHQ
IIVLAEGVMSGDEFAKTMKAAGDDSDLRVTNLGHLLRGGSPTARDRVLASRMGAYAVQLLKEGRGGLAVGVH
NEEMVESPILGLAEEGALFSLTDEGKIVVNNPHKADLRLAALNRDLANQSSK

GBS 328

GBS 328 belongs to the 5'-nucleotidase family. Nucleotide and amino acid sequences of GBS 328 sequenced from serotype V isolated strain 2603 V/R are set forth in Ref. 3 as SEQ ID 6015 and SEQ ID 6016. These sequences are set forth below as SEQ ID NOS 79 and 80:

SEQ ID NO. 79

ATGAAAAAGAAAATTATTTTGAAAAGTAGTGTTCTTGGTTTAGTCGCTGGGACTTCTATTATGTTCTCAAGC
GTGTTCGCGGACCAAGTCGGTGTCCAAGTTATAGGCGTCAATGACTTTCATGGTGCACTTGACAATACTGGA
ACAGCAAATATGCCTGATGGAAAAGTTGCTAATGCTGGTACTGCTGCTCAATTAGATGCTTATATGGATGAC
GCTCAAAAAGATTTCAAACAAACTAACCCTAATGGTGAAAGCATTAGGGTTCAAGCAGGCGATATGGTTGGA
GCAAGTCCAGCCAACTCTGGGCTTCTTCAAGATGAACCAACTGTCAAAAATTTTAATGCAATGAATGTTGAG
TATGGCACATTGGGTAACCATGAATTTGATGAAGGGTTGGCAGAATATAATCGTATCGTTACTGGTAAAGCC
CCTGCTCCAGATTCTAATATTAATAATATTACGAAATCATACCCACATGAAGCTGCAAAACAAGAAATTGTA
GTGGCAAATGTTATTGATAAAGTTAACAAACAAATTCCTTACAATTGGAAGCCTTACGCTATTAAAAATATT
CCTGTAAATAACAAAAGTGTGAACGTTGGCTTTATCGGGATTGTCACCAAAGACATCCCAAACCTTGTCTTA
CGTAAAAATTATGAACAATATGAATTTTTAGATGAAGCTGAAACAATCGTTAAATACGCCAAAGAATTACAA
GCTAAAAATGTCAAAGCTATTGTAGTTCTCGCACATGTACCTGCAACAAGTAAAAATGATATTGCTGAAGGT
GAAGCAGCAGAAATGATGAAAAAAGTCAATCAACTCTTCCCTGAAAATAGCGTAGATATTGTCTTTGCTGGA
CACAATCATCAATATACAAATGGTCTTGTTGGTAAAACTCGTATTGTACAAGCGCTCTCTCAAGGAAAAGCC
TATGCTGATGTACGTGGTGTCTTAGATACTGATACACAAGATTTCATTGAGACCCCTTCAGCTAAAGTAATT
GCAGTTGCTCCTGGTAAAAAAACAGGTAGTGCCGATATTCAAGCCATTGTTGACCAAGCTAATACTATCGTT
AAACAAGTAACAGAAGCTAAAATTGGTACTGCCGAGGTAAGTGTCATGATTACGCGTTCTGTTGATCAAGAT
AATGTTAGTCCGGTAGGCAGCCTCATCACAGAGGCTCAACTAGCAATTGCTCGAAAAAGCTGGCCAGATATC
GATTTTGCCATGACAAATAATGGTGGCATTCGTGCTGACTTACTCATCAAACCAGATGGAACAATCACCTGG
GGAGCTGCACAAGCAGTTCAACCTTTGGTAATATCTTACAAGTCGTCGAAATTACTGGTAGAGATCTTTAT
AAAGCACTCAACGAACAATACGACCAAAAACAAAATTTCTTCCTTCAAATAGCTGGTCTGCGATACACTTAC
ACAGATAATAAAGAGGGCGGGGAAGAAACACCATTTAAAGTTGTAAAAGCTTATAAATCAAATGGTGAGGAA
ATCAATCCTGATGCAAAATACAAATTAGTTATCAATGACTTTTTATTCGGTGGTGGTGATGGCTTTGCAAGC
TTCAGAAATGCCAAACTTCTAGGAGCCATTAACCCCGATACAGAGGTATTTATGGCCTATATCACTGATTTA
GAAAAAGCTGGTAAAAAAGTGAGCGTTCCAAATAATAAACCTAAAATCTATGTCACTATGAAGATGGTTAAT
GAAACTATTACACAAAATGATGGTACACATAGCATTATTAAGAAACTTTATTTAGATCGACAAGGAAATATT
GTAGCACAAGAGATTGTATCAGACACTTTAAACCAAACAAAATCAAAATCTACAAAAATCAACCCTGTAACT
ACAATTCACAAAAAACAATTACACCAATTTACAGCTATTAACCCTATGAGAAATTATGGCAAACCATCAAAC
TCCACTACTGTAAAATCAAAACAATTACCAAAAACAAACTCTGAATATGGACAATCATTCCTTATGTCTGTC
TTTGGTGTTGGACTTATAGGAATTGCTTTAAATACAAAGAAAAAACATATGAAA

SEQ ID NO. 80

MKKKIILKSSVLGLVAGTSIMFSSVFADQVGVQVIGVNDFHGALDNTGTANMPDGKVANAGTAAQLDAYMDD
AQKDFKQTNPNGESIRVQAGDMVGASPANSGLLQDEPTVKNFNAMNVEYGTLGNHEFDEGLAEYNRIVTGKA
PAPDSNINNITKSYPHEAAKQEIVVANVIDKVNKQIPYNWKPYAIKNIPVNNKSVNVGFIGIVTKDIPNLVL
RKNYEQYEFLDEAETIVKYAKELQAKNVKAIVVLAHVPATSKNDIAEGEAAEMMKKVNQLFPENSVDIVFAG
HNHQYTNGLVGKTRIVQALSQGKAYADVRGVLDTDTQDFIETPSAKVIAVAPGKKTGSADIQAIVDQANTIV
KQVTEAKIGTAEVSVMITRSVDQDNVSPVGSLITEAQLAIARKSWPDIDFAMTNNGGIRADLLIKPDGTITW
GAAQAVQPFGNILQVVEITGRDLYKALNEQYDQKQNFFLQIAGLRYTYTDNKEGGEETPFKVVKAYKSNGEE
INPDAKYKLVINDFLFGGGDGFASFRNAKLLGAINPDTEVFMAYITDLEKAGKKVSVPNNKPKIYVTMKMVN
ETITQNDGTHSIIKKLYLDRQGNIVAQEIVSDTLNQTKSKSTKINPVTTIHKKQLHQFTAINPMRNYGKPSN
STTVKSKQLPKTNSEYGQSFLMSVFGVGLIGIALNTKKKHMK

GBS 328 may contain an N-terminal leader or signal sequence region which is indicated by the underlined sequence at the beginning of SEQ ID NO: 80 above. In one embodiment, one or more amino

acids from the leader or signal sequence region of GBS 328 are removed. An example of such a GBS 328 fragment is set forth below as SEQ ID NO: 81.

SEQ ID NO: 81

HGALDNTGTANMPDGKVANAGTAAQLDAYMDDAQKDFKQTNPNGESIRVQAGDMVGASPANSGLLQDEPTVK
NFNAMNVEYGTLGNHEFDEGLAEYNRIVTGKAPAPDSNINNITKSYPHEAAKQEIVVANVIDKVNKQIPYNW
KPYAIKNIPVNNKSVNVGFIGIVTKDIPNLVLRKNYEQYEFLDEAETIVKYAKELQAKNVKAIVVLAHVPAT
SKNDIAEGEAAEMMKKVNQLFPENSVDIVFAGHNHQYTNGLVGKTRIVQALSQGKAYADVRGVLDTDTQDFI
ETPSAKVIAVAPGKKTGSADIQAIVDQANTIVKQVTEAKIGTAEVSVMITRSVDQDNVSPVGSLITEAQLAI
ARKSWPDIDFAMTNNGGIRADLLIKPDGTITWGAAQAVQPFGNILQVVEITGRDLYKALNEQYDQKQNFFLQ
IAGLRYTYTDNKEGGEETPFKVVKAYKSNGEEINPDAKYKLVINDFLFGGGDGFASFRNAKLLGAINPDTEV
FMAYITDLEKAGKKVSVPNNKPKIYVTMKMVNETITQNDGTHSIIKKLYLDRQGNIVAQEIVSDTLNQTKSK
STKINPVTTIHKKQLHQFTAINPMRNYGKPSNSTTVKSKQLPKTNSEYGQSFLMSVFGVGLIGIALNTKKKH
MK

GBS 328 may also contain a transmembrane and/or cytoplasmic domain region. In one embodiment, one or more amino acids from the transmembrane and/or cytoplasmic domain region of GBS 328 are removed. An example of such a GBS 328 fragment is set forth below as SEQ ID NO: 82.

SEQ ID NO: 82

MKKKIILKSSVLGLVAGTSIMFSSVFADQVGVQVIGVNDFHGALDNTGTANMPDGKVANAGTAAQLDAYMDD
AQKDFKQTNPNGESIRVQAGDMVGASPANSGLLQDEPTVKNFNAMNVEYGTLGNHEFDEGLAEYNRIVTGKA
PAPDSNINNITKSYPHEAAKQEIVVANVIDKVNKQIPYNWKPYAIKNIPVNNKSVNVGFIGIVTKDIPNLVL
RKNYEQYEFLDEAETIVKYAKELQAKNVKAIVVLAHVPATSKNDIAEGEAAEMMKKVNQLFPENSVDIVFAG
HNHQYTNGLVGKTRIVQALSQGKAYADVRGVLDTDTQDFIETPSAKVIAVAPGKKTGSADIQAIVDQANTIV
KQVTEAKIGTAEVSVMITRSVDQDNVSPVGSLITEAQLAIARKSWPDIDFAMTNNGGIRADLLIKPDGTITW
GAAQAVQPFGNILQVVEITGRDLYKALNEQYDQKQNFFLQIAGLRYTYTDNKEGGEETPFKVVKAYKSNGEE
INPDAKYKLVINDFLFGGGDGFASFRNAKLLGAINPDTEVFMAYITDLEKAGKKVSVPNNKPKIYVTMKMVN
ETITQNDGTHSIIKKLYLDRQGNIVAQEIVSDTLNQTKSKSTKINPVTTIHKKQLHQFTAINPMRNYGKPSN
STTVKS

In one embodiment, one or more amino acids from the leader or signal sequence region and one or more amino acids from the transmembrane or cytoplasmic region of GBS 328 are removed. An example of such a GBS 328 fragment is set forth below as SEQ ID NO: 83.

SEQ ID NO: 83

HGALDNTGTANMPDGKVANAGTAAQLDAYMDDAQKDFKQTNPNGESIRVQAGDMVGASPANSGLLQDEPTVK
NFNAMNVEYGTLGNHEFDEGLAEYNRIVTGKAPADSNINNITKSYPHEAAKQEIVVANVIDKVNKQIPYNW
KPYAIKNIPVNNKSVNVGFIGIVTKDIPNLVLRKNYEQYEFLDEAETIVKYAKELQAKNVKAIVVLAHVPAT
SKNDIAEGEAAEMMKKVNQLFPENSVDIVFAGHNHQYTNGLVGKTRIVQALSQGKAYADVRGVLDTDTQDFI
ETPSAKVIAVAPGKKTGSADIQAIVDQANTIVKQVTEAKIGTAEVSVMITRSVDQDNVSPVGSLITEAQLAI
ARKSWPDIDFAMTNNGGIRADLLIKPDGTITWGAAQAVQPFGNILQVVEITGRDLYKALNEQYDQKQNFFLQ
IAGLRYTYTDNKEGGEETPFKVVKAYKSNGEEINPDAKYKLVINDFLFGGGDGFASFRNAKLLGAINPDTEV
FMAYITDLEKAGKKVSVPNNKPKIYVTMKMVNETITQNDGTHSIIKKLYLDRQGNIVAQEIVSDTLNQTKSK
STKINPVTTIHKKQLHQFTAINPMRNYGKPSNSTTVKS

GBS 656

GBS 656 refers to a putative DNA-entry nuclease. Nucleotide and amino acid sequences of GBS 656 sequenced from serotype V isolated strain 2603 V/R are set forth in Ref. 3 as SEQ ID 9323 and SEQ ID 9324. These sequences are set forth below as SEQ ID NOS 84 and 85:

SEQ ID NO. 84

ATGAAAAGATTACATAAACTGTTTATAACCGTAATTGCTACATTAGGTATGTTGGGGGTAATGACCTTTGGT
CTTCCAACGCAGCCGCAAAACGTAACGCCGATAGTACATGCTGATGTCAATTCATCTGTTGATACGAGCCAG

GAATTTCAAAATAATTTAAAAAATGCTATTGGTAACCTACCATTTCAATATGTTAATGGTATTTATGAATTA
AATAATAATCAGACAAATTTAAATGCTGATGTCAATGTTAAAGCGTATGTTCAAAATACAATTGACAATCAA
CAAAGACTATCAACTGCTAATGCAATGCTTGATAGAACCATTCGTCAATATCAAAATCGCAGAGATACCACT
CTTCCCGATGCAAATTGGAAACCATTAGGTTGGCATCAAGTAGCTACTAATGACCATTATGGACATGCAGTC
GACAAGGGGCATTTAATTGCCTATGCTTTAGCTGGAAATTTCAAAGGTTGGGATGCTTCCGTGTCAAATCCT
CAAAATGTTGTCACACAAACAGCTCATTCCAACCAATCAAATCAAAAAATCAATCGTGGACAAAATTATTAT
GAAAGCTTAGTTCGTAAGGCGGTTGACCAAAACAAACGTGTTCGTTACCGTGTAACTCCATTGTACCGTAAT
GATACTGATTTAGTTCCATTTGCAATGCACCTAGAAGCTAAATCACAAGATGGCACATTAGAATTTAATGTT
GCTATTCCAAACACACAAGCATCATACACTATGGATTATGCAACAGGAGAAATAACACTAAAT

SEQ ID NO. 85
MKRLHKLFITVIATLGMLGVMTFGLPTQPQNVTPIVHADVNSSVDTSQEFQNNLKNAIGNLPFQYVNGIYEL
NNNQTNLNADVNVKAYVQNTIDNQQRLSTANAMLDRTIRQYQNRRDTTLPDANWKPLGWHQVATNDHYGHAV
DKGHLIAYALAGNFKGWDASVSNPQNVVTQTAHSNQSNQKINRGQNYYESLVRKAVDQNKRVRYRVTPLYRN
DTDLVPFAMHLEAKSQDGTLEFNVAIPNTQASYTMDYATGEITLN

The compositions of the invention may also include combinations including one or more known GBS antigens in combination with GBS 80.

There is an upper limit to the number of GBS antigens which will be in the compositions of the invention. Preferably, the number of GBS antigens in a composition of the invention is less than 20, less than 19, less than 18, less than 17, less than 16, less than 15, less than 14, less than 13, less than 12, less than 11, less than 10, less than 9, less than 8, less than 7, less than 6, less than 5, less than 4, or less than 3. Still more preferably, the number of GBS antigens in a composition of the invention is less than 6, less than 5, or less than 4. Still more preferably, the number of GBS antigens in a composition of the invention is 3.

The GBS antigens used in the invention are preferably isolated, i.e., separate and discrete, from the whole organism with which the molecule is found in nature or, when the polynucleotide or polypeptide is not found in nature, is sufficiently free of other biological macromolecules so that the polynucleotide or polypeptide can be used for its intended purpose.

Fusion Proteins

The GBS antigens used in the invention may be present in the composition as individual separate polypeptides, but it is preferred that at least two (*i.e.* 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, or 18) of the antigens are expressed as a single polypeptide chain (a "hybrid" or "fusion" polypeptide). Such fusion polypeptides offer two principal advantages: first, a polypeptide that may be unstable or poorly expressed on its own can be assisted by adding a suitable fusion partner that overcomes the problem; second, commercial manufacture is simplified as only one expression and purification need be employed in order to produce two polypeptides which are both antigenically useful.

The fusion polypeptide may comprise two or more polypeptide sequences from the group consisting of GBS 80, GBS 91, GBS 104, GBS 184, GBS 276, GBS 305, GBS 322, GBS 330, GBS 338, GBS 361, GBS 404, GBS 690 and GBS 691. Preferably, the polypeptide sequences are selected from the group consisting of GBS 80, GBS 104 and GBS 322. Most preferably, the fusion peptide includes a polypeptide sequence from GBS 80. Accordingly, the invention includes a fusion peptide comprising a first amino acid sequence and a second amino acid sequence, wherein said first and second amino acid sequences are

selected from a GBS antigen or a fragment thereof of the above antigen group. Preferably, the first and second amino acid sequences in the fusion polypeptide comprise different epitopes.

Hybrids (or fusions) consisting of amino acid sequences from two, three, four, five, six, seven, eight, nine, or ten GBS antigens are preferred. In particular, hybrids consisting of amino acid sequences from two, three, four, or five GBS antigens are preferred.

Different hybrid polypeptides may be mixed together in a single formulation. Within such combinations, a GBS antigen may be present in more than one hybrid polypeptide and/or as a non-hybrid polypeptide. It is preferred, however, that an antigen is present either as a hybrid or as a non-hybrid, but not as both.

Hybrid polypeptides can be represented by the formula **NH_2-A-{-X-L-}$_n$-B-COOH**, wherein: X is an amino acid sequence of a GBS antigen or a fragment thereof from the antigen group set forth above; L is an optional linker amino acid sequence; A is an optional N-terminal amino acid sequence; B is an optional C-terminal amino acid sequence; and *n* is 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14 or 15.

If a -X- moiety has a leader peptide sequence in its wild-type form, this may be included or omitted in the hybrid protein. In some embodiments, the leader peptides will be deleted except for that of the -X- moiety located at the N-terminus of the hybrid protein *i.e.* the leader peptide of X_1 will be retained, but the leader peptides of X_2 ... X_n will be omitted. This is equivalent to deleting all leader peptides and using the leader peptide of X_1 as moiety -A-.

For each *n* instances of {-X-L-}, linker amino acid sequence -L- may be present or absent. For instance, when *n*=2 the hybrid may be NH_2-X_1-L_1-X_2-L_2-COOH, NH_2-X_1-X_2-COOH, NH_2-X_1-L_1-X_2-COOH, NH_2-X_1-X_2-L_2-COOH, *etc.* Linker amino acid sequence(s) -L- will typically be short (*e.g.* 20 or fewer amino acids *i.e.* 19, 18, 17, 16, 15, 14, 13, 12, 11, 10, 9, 8, 7, 6, 5, 4, 3, 2, 1). Examples comprise short peptide sequences which facilitate cloning, poly-glycine linkers (*i.e.* comprising Gly_n where $n = 2, 3, 4, 5, 6, 7, 8, 9$, 10 or more), and histidine tags (*i.e.* His_n where $n = 3, 4, 5, 6, 7, 8, 9, 10$ or more). Other suitable linker amino acid sequences will be apparent to those skilled in the art. A useful linker is GSGGGG, with the Gly-Ser dipeptide being formed from a *Bam*HI restriction site, thus aiding cloning and manipulation, and the $(Gly)_4$ tetrapeptide being a typical poly-glycine linker.

-A- is an optional N-terminal amino acid sequence. This will typically be short (*e.g.* 40 or fewer amino acids *i.e.* 39, 38, 37, 36, 35, 34, 33, 32, 31, 30, 29, 28, 27, 26, 25, 24, 23, 22, 21, 20, 19, 18, 17, 16, 15, 14, 13, 12, 11, 10, 9, 8, 7, 6, 5, 4, 3, 2, 1). Examples include leader sequences to direct protein trafficking, or short peptide sequences which facilitate cloning or purification (*e.g.* histidine tags *i.e.* His_n where $n = 3, 4, 5, 6, 7, 8, 9, 10$ or more). Other suitable N-terminal amino acid sequences will be apparent to those skilled in the art. If X_1 lacks its own N-terminus methionine, -A- is preferably an oligopeptide (*e.g.* with 1, 2, 3, 4, 5, 6, 7 or 8 amino acids) which provides a N-terminus methionine.

-B- is an optional C-terminal amino acid sequence. This will typically be short (*e.g.* 40 or fewer amino acids *i.e.* 39, 38, 37, 36, 35, 34, 33, 32, 31, 30, 29, 28, 27, 26, 25, 24, 23, 22, 21, 20, 19, 18, 17, 16, 15, 14, 13, 12, 11, 10, 9, 8, 7, 6, 5, 4, 3, 2, 1). Examples include sequences to direct protein trafficking, short

peptide sequences which facilitate cloning or purification (*e.g.* comprising histidine tags *i.e.* His_n where n = 3, 4, 5, 6, 7, 8, 9, 10 or more), or sequences which enhance protein stability. Other suitable C-terminal amino acid sequences will be apparent to those skilled in the art.

Most preferably, n is 2 or 3.

Nucleic Acids

The invention also provides nucleic acid encoding the GBS antigens and/or the hybrid fusion polypeptides of the invention. Furthermore, the invention provides nucleic acid which can hybridise to these nucleic acids, preferably under "high stringency" conditions (*e.g.* 65°C in a 0.1xSSC, 0.5% SDS solution).

Polypeptides of the invention can be prepared by various means (*e.g.* recombinant expression, purification from cell culture, chemical synthesis, *etc.*) and in various forms (*e.g.* native, fusions, non-glycosylated, lipidated, *etc.*). They are preferably prepared in substantially pure form (*i.e.* substantially free from other GAS or host cell proteins).

Nucleic acid according to the invention can be prepared in many ways (*e.g.* by chemical synthesis, from genomic or cDNA libraries, from the organism itself, *etc.*) and can take various forms (*e.g.* single stranded, double stranded, vectors, probes, *etc.*). They are preferably prepared in substantially pure form (*i.e.* substantially free from other GBS or host cell nucleic acids).

The term "nucleic acid" includes DNA and RNA, and also their analogues, such as those containing modified backbones (*e.g.* phosphorothioates, *etc.*), and also peptide nucleic acids (PNA), *etc.* The invention includes nucleic acid comprising sequences complementary to those described above (*e.g.* for antisense or probing purposes).

The invention also provides a process for producing a polypeptide of the invention, comprising the step of culturing a host cell transformed with nucleic acid of the invention under conditions which induce polypeptide expression.

The invention provides a process for producing a polypeptide of the invention, comprising the step of synthesising at least part of the polypeptide by chemical means.

The invention provides a process for producing nucleic acid of the invention, comprising the step of amplifying nucleic acid using a primer-based amplification method (*e.g.* PCR).

The invention provides a process for producing nucleic acid of the invention, comprising the step of synthesising at least part of the nucleic acid by chemical means.

Purification and Recombinant Expression

The GBS antigens of the invention may be isolated from *Streptococcus agalactiae*, or they may be recombinantly produced, for instance, in a heterologous host. Preferably, the GBS antigens are prepared using a heterologous host. The heterologous host may be prokaryotic (*e.g.* a bacterium) or eukaryotic. It is preferably *E.coli*, but other suitable hosts include *Bacillus subtilis, Vibrio cholerae, Salmonella typhi,*

Salmonella typhimurium, Neisseria lactamica, Neisseria cinerea, Mycobacteria (*e.g. M.tuberculosis*), yeasts, *etc.*

Recombinant production of polypeptides is facilitated by adding a tag protein to the GBS antigen to be expressed as a fusion protein comprising the tag protein and the GBS antigen. Such tag proteins can facilitate purification, detection and stability of the expressed protein. Tag proteins suitable for use in the invention include a polyarginine tag (Arg-tag), polyhistidine tag (His-tag), FLAG-tag, Strep-tag, c-myc-tag, S-tag, calmodulin-binding peptide, cellulose-binding domain, SBP-tag,, chitin-binding domain, glutathione S-transferase-tag (GST), maltose-binding protein, transcription termination anti-terminiantion factor (NusA), *E. coli* thioredoxin (TrxA) and protein disulfide isomerase I (DsbA). Preferred tag proteins include His-tag and GST. A full discussion on the use of tag proteins can be found at Ref. 3.

After purification, the tag proteins may optionally be removed from the expressed fusion protein, i.e., by specifically tailored enzymatic treatments known in the art. Commonly used proteases include enterokinase, tobacco etch virus (TEV), thrombin, and factor X_a.

GBS polysaccharides

The compositions of the invention may be further improved by including GBS polysaccharides. Preferably, the GBS antigen and the saccharide each contribute to the immunological response in a recipient. The combination is particularly advantageous where the saccharide and polypeptide provide protection from different GBS serotypes.

The combined antigens may be present as a simple combination where separate saccharide and polypeptide antigens are administered together, or they may be present as a conjugated combination, where the saccharide and polypeptide antigens are covalently linked to each other.

Thus the invention provides an immunogenic composition comprising (i) one or more GBS polypeptide antigens and (ii) one or more GBS saccharide antigens. The polypeptide and the polysaccharide may advantageously be covalently linked to each other to form a conjugate.

Between them, the combined polypeptide and saccharide antigens preferably cover (or provide protection from) two or more GBS serotypes (*e.g.* 2, 3, 4, 5, 6, 7, 8 or more serotypes). The serotypes of the polypeptide and saccharide antigens may or may not overlap. For example, the polypeptide might protect against serogroup II or V, while the saccharide protects against either serogroups Ia, Ib, or III. Preferred combinations protect against the following groups of serotypes: (1) serotypes Ia and Ib, (2) serotypes Ia and II, (3) serotypes Ia and III, (4) serotypes Ia and IV, (5) serotypes Ia and V, (6) serotypes Ia and VI, (7) serotypes Ia and VII, (8) serotypes Ia and VIII, (9) serotypes Ib and II, (10) serotypes Ib and III, (11) serotypes Ib and IV, (12) serotypes Ib and V, (13) serotypes Ib and VI, (14) serotypes Ib and VII, (15) serotypes Ib and VIII, 16) serotypes II and III, (17) serotypes II and IV, (18) serotypes II and V, (19) serotypes II and VI, (20) serotypes II and VII, (21) serotypes II and VII, (22) serotypes III and IV, (23) serotypes III and V, (24) serotypes III and VI, (25) serotypes III and VII, (26) serotypes III and VIII, (27) serotypes IV and V, (28) serotypes IV and VI, (29) serotypes IV and VII, (30) serotypes IV and VIII, (31)

serotypes V and VI, (32) serotypes V and VII, (33) serotypes V and VIII, (34) serotypes VI and VII, (35) serotypes VI and VIII, and (36) serotypes VII and VIII.

Still more preferably, the combinations protect against the following groups of serotypes: (1) serotypes Ia and II, (2) serotypes Ia and V, (3) serotypes Ib and II, (4) serotypes Ib and V, (5) serotypes III and II, and (6) serotypes III and V. Most preferably, the combinations protect against serotypes III and V.

Protection against serotypes II and V is preferably provided by polypeptide antigens. Protection against serotypes Ia, Ib and/or III may be polypeptide or saccharide antigens.

In one embodiment, the immunogenic composition comprises a GBS saccharide antigen and at least two GBS polypeptide antigens or fragments thereof, wherein said GBS saccharide antigen comprises a saccharide selected from GBS serotype Ia, Ib, and III, and wherein said GBS polypeptide antigens comprise a combination of at least two polypeptide or a fragment thereof selected from the antigen group consisting of GBS 80, GBS 91, GBS 104, GBS 184, GBS 276, GBS 305, GBS 322, GBS 330, GBS 338, GBS 361, GBS 404, GBS 690, and GBS 691. Preferably, the combination includes one or more of GBS 80, GBS 104 and GBS 322. Still more preferably, the combination includes GBS 80 or a fragment thereof.

In certain embodiments, the compositions of the invention do not include a GBS polysaccharide. In certain embodiments, the combination does not include one or more of the GBS antigens selected from the group consisting of GBS 4, GBS 22, GBS 85, GBS 338 and GBS 361.

Immunogenic compositions and medicaments

Compositions of the invention are preferably immunogenic compositions, and are more preferably vaccine compositions. The pH of the composition is preferably between 6 and 8, preferably about 7. The pH may be maintained by the use of a buffer. The composition may be sterile and/or pyrogen-free. The composition may be isotonic with respect to humans.

Vaccines according to the invention may either be prophylactic (*i.e.* to prevent infection) or therapeutic (*i.e.* to treat infection), but will typically be prophylactic. Accordingly, the invention includes a method for the therapeutic or prophylactic treatment of a *Streptococcus agalactiae* infection in an animal susceptible to streptococcal infection comprising administering to said animal a therapeutic or prophylactic amount of the immunogenic compositions of the invention.

The invention also provides a composition of the invention for use as a medicament. The medicament is preferably able to raise an immune response in a mammal (*i.e.* it is an immunogenic composition) and is more preferably a vaccine.

The invention also provides the use of the compositions of the invention in the manufacture of a medicament for raising an immune response in a mammal. The medicament is preferably a vaccine.

The invention also provides for a kit comprising a first component comprising a combination of GBS antigens.

The invention also provides a delivery device pre-filled with the immunogenic compositions of the invention.

The invention also provides a method for raising an immune response in a mammal comprising the step of administering an effective amount of a composition of the invention. The immune response is preferably protective and preferably involves antibodies and/or cell-mediated immunity. The method may raise a booster response.

The mammal is preferably a human. Where the vaccine is for prophylactic use, the human is preferably a female (either of child bearing age or a teenager). Alternatively, the human may be elderly (e.g., over the age of 50, 55, 60, 65, 70 or 75) and may have an underlying disease such as diabetes or cancer. Where the vaccine is for therapeutic use, the human is preferably a pregnant female or an elderly adult.

These uses and methods are preferably for the prevention and/or treatment of a disease caused by *Streptococcus agalactiae*. The compositions may also be effective against other streptococcal bacteria.

One way of checking efficacy of therapeutic treatment involves monitoring GBS infection after administration of the composition of the invention. One way of checking efficacy of prophylactic treatment involves monitoring immune responses against the GBS antigens in the compositions of the invention after administration of the composition.

Compositions of the invention will generally be administered directly to a patient. Direct delivery may be accomplished by parenteral injection (*e.g.* subcutaneously, intraperitoneally, intradermally, intravenously, intramuscularly, or to the interstitial space of a tissue), or by rectal, oral (*e.g.* tablet, spray), vaginal, topical, transdermal {*e.g.* see ref. 4} or transcutaneous {*e.g.* see refs. 5 & 6}, intranasal {*e.g.* see ref. 7}, ocular, aural, pulmonary or other mucosal administration.

The invention may be used to elicit systemic and/or mucosal immunity.

Dosage treatment can be a single dose schedule or a multiple dose schedule. Multiple doses may be used in a primary immunisation schedule and/or in a booster immunisation schedule. In a multiple dose schedule the various doses may be given by the same or different routes *e.g.* a parenteral prime and mucosal boost, a mucosal prime and parenteral boost, *etc.*

The compositions of the invention may be prepared in various forms. For example, the compositions may be prepared as injectables, either as liquid solutions or suspensions. Solid forms suitable for solution in, or suspension in, liquid vehicles prior to injection can also be prepared (*e.g.* a lyophilised composition). The composition may be prepared for topical administration *e.g.* as an ointment, cream or powder. The composition may be prepared for oral administration *e.g.* as a tablet or capsule, as a spray, or as a syrup (optionally flavoured). The composition may be prepared for pulmonary administration *e.g.* as an inhaler, using a fine powder or a spray. The composition may be prepared as a suppository or pessary. The composition may be prepared for nasal, aural or ocular administration *e.g.* as drops. The composition may be in kit form, designed such that a combined composition is reconstituted just prior to administration to a patient. Such kits may comprise one or more antigens in liquid form and one or more lyophilised antigens.

Immunogenic compositions used as vaccines comprise an immunologically effective amount of antigen(s), as well as any other components, as needed. By 'immunologically effective amount', it is meant

that the administration of that amount to an individual, either in a single dose or as part of a series, is effective for treatment or prevention. This amount varies depending upon the health and physical condition of the individual to be treated, age, the taxonomic group of individual to be treated (*e.g.* non-human primate, primate, *etc.*), the capacity of the individual's immune system to synthesise antibodies, the degree of protection desired, the formulation of the vaccine, the treating doctor's assessment of the medical situation, and other relevant factors. It is expected that the amount will fall in a relatively broad range that can be determined through routine trials.

Further Components of the Composition

The composition of the invention will typically, in addition to the components mentioned above, comprise one or more 'pharmaceutically acceptable carriers', which include any carrier that does not itself induce the production of antibodies harmful to the individual receiving the composition. Suitable carriers are typically large, slowly metabolised macromolecules such as proteins, polysaccharides, polylactic acids, polyglycolic acids, polymeric amino acids, amino acid copolymers, and lipid aggregates (such as oil droplets or liposomes). Such carriers are well known to those of ordinary skill in the art. The vaccines may also contain diluents, such as water, saline, glycerol, *etc.* Additionally, auxiliary substances, such as wetting or emulsifying agents, pH buffering substances, and the like, may be present. A thorough discussion of pharmaceutically acceptable excipients is available in reference 8.

Vaccines of the invention may be administered in conjunction with other immunoregulatory agents. In particular, compositions will usually include an adjuvant.

Preferred further adjuvants include, but are not limited to, one or more of the following set forth below:

A. Mineral Containing Compositions

Mineral containing compositions suitable for use as adjuvants in the invention include mineral salts, such as aluminium salts and calcium salts. The invention includes mineral salts such as hydroxides (*e.g.* oxyhydroxides), phosphates (*e.g.* hydroxyphoshpates, orthophosphates), sulphates, *etc.* {*e.g.* see chapters 8 & 9 of ref. 9}), or mixtures of different mineral compounds, with the compounds taking any suitable form (*e.g.* gel, crystalline, amorphous, *etc.*), and with adsorption being preferred. The mineral containing compositions may also be formulated as a particle of metal salt. See ref. 10.

B. Oil-Emulsions

Oil-emulsion compositions suitable for use as adjuvants in the invention include squalene-water emulsions, such as MF59 (5% Squalene, 0.5% Tween 80, and 0.5% Span 85, formulated into submicron particles using a microfluidizer). See WO90/14837. See also, Frey et al., "Comparison of the safety, tolerability, and immunogenicity of a MF59-adjuvanted influenza vaccine and a non-adjuvanted influenza vaccine in non-elderly adults", Vaccine (2003) 21:4234 – 4237.

Particularly preferred adjuvants for use in the compositions are submicron oil-inwater emulsions. Preferred submicron oil-in-water emulsions for use herein are squalene/water emulsions

optionally containing varying amounts of MTP-PE, such as a submicron oil-in-water emulsion containing 4-5% w/v squalene, 0.25-1.0% w/v Tween 80 ™ (polyoxyelthylenesorbitan monooleate), and/or 0.25-1.0% Span 85™ (sorbitan trioleate), and, optionally, N-acetylmuramyl-L-alanyl-D-isogluatminyl-L-alanine-2-(1'-2'-dipalmitoyl-*sn*-glycero-3-huydroxyphosphophoryloxy)-ethylamine (MTP-PE), for example, the submicron oil-in-water emulsion known as "MF59" (International Publication No. WO 90/14837; U.S. Patent Nos. 6,299,884 and 6,451,325, incorporated herein by reference in their entireties; and Ott et al., "MF59 -- Design and Evaluation of a Safe and Potent Adjuvant for Human Vaccines" in *Vaccine Design: The Subunit and Adjuvant Approach* (Powell, M.F. and Newman, M.J. eds.) Plenum Press, New York, 1995, pp. 277-296). MF59 contains 4-5% w/v Squalene (e.g., 4.3%), 0.25-0.5% w/v Tween 80™, and 0.5% w/v Span 85™ and optionally contains various amounts of MTP-PE, formulated into submicron particles using a microfluidizer such as Model 110Y microfluidizer (Microfluidics, Newton, MA). For example, MTP-PE may be present in an amount of about 0-500 μg/dose, more preferably 0-250 μg/dose and most preferably, 0-100 μg/dose. As used herein, the term "MF59-0" refers to the above submicron oil-in-water emulsion lacking MTP-PE, while the term MF59-MTP denotes a formulation that contains MTP-PE. For instance, "MF59-100" contains 100 μg MTP-PE per dose, and so on. MF69, another submicron oil-in-water emulsion for use herein, contains 4.3% w/v squalene, 0.25% w/v Tween 80™, and 0.75% w/v Span 85™ and optionally MTP-PE. Yet another submicron oil-in-water emulsion is MF75, also known as SAF, containing 10% squalene, 0.4% Tween 80™, 5% pluronic-blocked polymer L121, and thr-MDP, also microfluidized into a submicron emulsion. MF75-MTP denotes an MF75 formulation that includes MTP, such as from 100-400 μg MTP-PE per dose.

Submicron oil-in-water emulsions, methods of making the same and immunostimulating agents, such as muramyl peptides, for use in the compositions, are described in detail in International Publication No. WO 90114837 and U.S. Patent Nos. 6,299,884 and 6,45 1,325, incorporated herein by reference in their entireties.

Complete Freund's adjuvant (CFA) and incomplete Freund's adjuvant (IFA) may also be used as adjuvants in the invention.

C. Saponin Formulations

Saponin formulations, may also be used as adjuvants in the invention. Saponins are a heterologous group of sterol glycosides and triterpenoid glycosides that are found in the bark, leaves, stems, roots and even flowers of a wide range of plant species. Saponin from the bark of the *Quillaia saponaria* Molina tree have been widely studied as adjuvants. Saponin can also be commercially obtained from *Smilax ornata* (sarsaprilla), *Gypsophilla paniculata* (brides veil), and *Saponaria officianalis* (soap root). Saponin adjuvant formulations include purified formulations, such as QS21, as well as lipid formulations, such as ISCOMs.

Saponin compositions have been purified using High Performance Thin Layer Chromatography (HP-LC) and Reversed Phase High Performance Liquid Chromatography (RP-HPLC). Specific purified fractions using these techniques have been identified, including QS7, QS17, QS18, QS21, QH-A, QH-B and QH-C. Preferably, the saponin is QS21. A method of production of QS21 is disclosed in U.S. Patent No. 5,057,540. Saponin formulations may also comprise a sterol, such as cholesterol (see WO 96/33739). Combinations of saponins and cholesterols can be used to form unique particles called Immunostimulating Complexs (ISCOMs). ISCOMs typically also include a phospholipid such as phosphatidylethanolamine or phosphatidylcholine. Any known saponin can be used in ISCOMs. Preferably, the ISCOM includes one or more of Quil A, QHA and QHC. ISCOMs are further described in EP 0 109 942, WO 96/11711 and WO 96/33739. Optionally, the ISCOMS may be devoid of additional detergent. See ref. 11.

A review of the development of saponin based adjuvants can be found at ref. 12.

C. Virosomes and Virus Like Particles (VLPs)

Virosomes and Virus Like Particles (VLPs) can also be used as adjuvants in the invention. These structures generally contain one or more proteins from a virus optionally combined or formulated with a phospholipid. They are generally non-pathogenic, non-replicating and generally do not contain any of the native viral genome. The viral proteins may be recombinantly produced or isolated from whole viruses. These viral proteins suitable for use in virosomes or VLPs include proteins derived from influenza virus (such as HA or NA), Hepatitis B virus (such as core or capsid proteins), Hepatitis E virus, measles virus, Sindbis virus, Rotavirus, Foot-and-Mouth Disease virus, Retrovirus, Norwalk virus, human Papilloma virus, HIV, RNA-phages, Qß-phage (such as coat proteins), GA-phage, fr-phage, AP205 phage, and Ty (such as retrotransposon Ty protein p1). VLPs are discussed further in WO 03/024480, WO 03/024481, and Refs. 13, 14, 15 and 16. Virosomes are discussed further in, for example, Ref. 17

D. Bacterial or Microbial Derivatives

Adjuvants suitable for use in the invention include bacterial or microbial derivatives such as:

(1) *Non-toxic derivatives of enterobacterial lipopolysaccharide (LPS)*

Such derivatives include Monophosphoryl lipid A (MPL) and 3-O-deacylated MPL (3dMPL). 3dMPL is a mixture of 3 De-O-acylated monophosphoryl lipid A with 4, 5 or 6 acylated chains. A preferred "small particle" form of 3 De-O-acylated monophosphoryl lipid A is disclosed in EP 0 689 454. Such "small particles" of 3dMPL are small enough to be sterile filtered through a 0.22 micron membrane (see EP 0 689 454). Other non-toxic LPS derivatives include monophosphoryl lipid A mimics, such as aminoalkyl glucosaminide phosphate derivatives *e.g.* RC-529. See Ref. 18.

(2) *Lipid A Derivatives*

Lipid A derivatives include derivatives of lipid A from *Escherichia coli* such as OM-174. OM-174 is described for example in Ref. 19 and 20.

(3) *Immunostimulatory oligonucleotides*

Immunostimulatory oligonucleotides suitable for use as adjuvants in the invention include nucleotide sequences containing a CpG motif (a sequence containing an unmethylated cytosine followed by

guanosine and linked by a phosphate bond). Bacterial double stranded RNA or oligonucleotides containing palindromic or poly(dG) sequences have also been shown to be immunostimulatory.

The CpG's can include nucleotide modifications/analogs such as phosphorothioate modifications and can be double-stranded or single-stranded. Optionally, the guanosine may be replaced with an analog such as 2'-deoxy-7-deazaguanosine. See ref. 21, WO 02/26757 and WO 99/62923 for examples of possible analog substitutions. The adjuvant effect of CpG oligonucleotides is further discussed in Refs. 22, 23, WO 98/40100, U.S. Patent No. 6,207,646, U.S. Patent No. 6,239,116, and U.S. Patent No. 6,429,199.

The CpG sequence may be directed to TLR9, such as the motif GTCGTT or TTCGTT. See ref. 24. The CpG sequence may be specific for inducing a Th1 immune response, such as a CpG-A ODN, or it may be more specific for inducing a B cell response, such a CpG-B ODN. CpG-A and CpG-B ODNs are discussed in refs. 25, 26 and WO 01/95935. Preferably, the CpG is a CpG-A ODN.

Preferably, the CpG oligonucleotide is constructed so that the 5' end is accessible for receptor recognition. Optionally, two CpG oligonucleotide sequences may be attached at their 3' ends to form "immunomers". See, for example, refs. 27, 28, 29 and WO 03/035836.

(4) *ADP-ribosylating toxins and detoxified derivatives thereof.*

Bacterial ADP-ribosylating toxins and detoxified derivatives thereof may be used as adjuvants in the invention. Preferably, the protein is derived from *E. coli* (i.e., E. coli heat labile enterotoxin "LT), cholera ("CT"), or pertussis ("PT"). The use of detoxified ADP-ribosylating toxins as mucosal adjuvants is described in WO 95/17211 and as parenteral adjuvants in WO 98/42375. Preferably, the adjuvant is a detoxified LT mutant such as LT-K63.

E. Human Immunomodulators

Human immunomodulators suitable for use as adjuvants in the invention include cytokines, such as interleukins (*e.g.* IL-1, IL-2, IL-4, IL-5, IL-6, IL-7, IL-12, *etc.*), interferons (*e.g.* interferon-γ), macrophage colony stimulating factor, and tumor necrosis factor.

F. Bioadhesives and Mucoadhesives

Bioadhesives and mucoadhesives may also be used as adjuvants in the invention. Suitable bioadhesives include esterified hyaluronic acid microspheres (Ref. 30) or mucoadhesives such as cross-linked derivatives of poly(acrylic acid), polyvinyl alcohol, polyvinyl pyrollidone, polysaccharides and carboxymethylcellulose. Chitosan and derivatives thereof may also be used as adjuvants in the invention. E.g., ref. 31.

G. Microparticles

Microparticles may also be used as adjuvants in the invention. Microparticles (*i.e.* a particle of ~100nm to ~150μm in diameter, more preferably ~200nm to ~30μm in diameter, and most preferably ~500nm to ~10μm in diameter) formed from materials that are biodegradable and non-toxic (*e.g.* a poly(α-hydroxy acid), a polyhydroxybutyric acid, a polyorthoester, a polyanhydride, a polycaprolactone, *etc.*), with poly(lactide-co-glycolide) are preferred, optionally treated to have a negatively-charged surface (*e.g.* with SDS) or a positively-charged surface (*e.g.* with a cationic detergent, such as CTAB).

H. Liposomes

Examples of liposome formulations suitable for use as adjuvants are described in U.S. Patent No. 6,090,406, U.S. Patent No. 5,916,588, and EP 0 626 169.

I. Polyoxyethylene ether and Polyoxyethylene Ester Formulations

Adjuvants suitable for use in the invention include polyoxyethylene ethers and polyoxyethylene esters. Ref. 32. Such formulations further include polyoxyethylene sorbitan ester surfactants in combination with an octoxynol (Ref. 33) as well as polyoxyethylene alkyl ethers or ester surfactants in combination with at least one additional non-ionic surfactant such as an octoxynol (Ref. 34).

Preferred polyoxyethylene ethers are selected from the following group: polyoxyethylene-9-lauryl ether (laureth 9), polyoxyethylene-9-steoryl ether, polyoxytheylene-8-steoryl ether, polyoxyethylene-4-lauryl ether, polyoxyethylene-35-lauryl ether, and polyoxyethylene-23-lauryl ether.

J. Polyphosphazene (PCPP)

PCPP formulations are described, for example, in Ref. 35 and 36.

K. Muramyl peptides

Examples of muramyl peptides suitable for use as adjuvants in the invention include N-acetyl-muramyl-L-threonyl-D-isoglutamine (thr-MDP), N-acetyl-normuramyl-L-alanyl-D-isoglutamine (nor-MDP), and N-acetylmuramyl-L-alanyl-D-isoglutaminyl-L-alanine-2-(1'-2'-dipalmitoyl-*sn*-glycero-3-hydroxyphosphoryloxy)-ethylamine MTP-PE).

L. Imidazoquinolone Compounds.

Examples of imidazoquinolone compounds suitable for use adjuvants in the invention include Imiquamod and its homologues, described further in Ref. 37 and 38.

The invention may also comprise combinations of aspects of one or more of the adjuvants identified above. For example, the following adjuvant compositions may be used in the invention:

(1) a saponin and an oil-in-water emulsion (ref. 39);

(2) a saponin (e.g., QS21) + a non-toxic LPS derivative (e.g., 3dMPL) (see WO 94/00153);

(3) a saponin (e.g., QS21) + a non-toxic LPS derivative (e.g., 3dMPL) + a cholesterol;

(4) a saponin (*e.g.* QS21) + 3dMPL + IL-12 (optionally + a sterol) (Ref. 40);

(5) combinations of 3dMPL with, for example, QS21 and/or oil-in-water emulsions (Ref. 41);

(6) SAF, containing 10% Squalane, 0.4% Tween 80, 5% pluronic-block polymer L121, and thr-MDP, either microfluidized into a submicron emulsion or vortexed to generate a larger particle size emulsion.

(7) Ribi™ adjuvant system (RAS), (Ribi Immunochem) containing 2% Squalene, 0.2% Tween 80, and one or more bacterial cell wall components from the group consisting of monophosphorylipid A (MPL), trehalose dimycolate (TDM), and cell wall skeleton (CWS), preferably MPL + CWS (Detox™); and

(8) one or more mineral salts (such as an aluminum salt) + a non-toxic derivative of LPS (such as 3dPML).

Aluminium salts and MF59 are preferred adjuvants for parenteral immunisation. Mutant bacterial toxins are preferred mucosal adjuvants.

The composition may include an antibiotic.

Further antigens

The compositions of the invention may further comprise one or more additional non-GBS antigens, including additional bacterial, viral or parasitic antigens.

In another embodiment, the GBS antigen combinations of the invention are combined with one or more additional, non-GBS antigens suitable for use in a vaccine designed to protect elderly or immunocomprised individuals. For example, the GBS antigen combinations may be combined with an antigen derived from the group consisting of *Enterococcus faecalis, Staphylococcus aureus, Staphylococcus epidermis, Pseudomonas aeruginosa, Legionella pneumophila, Listeria monocytogenes, Neisseria meningitides,* influenza, and Parainfluenza virus ('PIV').

Where a saccharide or carbohydrate antigen is used, it is preferably conjugated to a carrier protein in order to enhance immunogenicity {*e.g.* refs. 42 to 51}. Preferred carrier proteins are bacterial toxins or toxoids, such as diphtheria or tetanus toxoids. The CRM_{197} diphtheria toxoid is particularly preferred {52}. Other carrier polypeptides include the *N.meningitidis* outer membrane protein {53}, synthetic peptides {54, 55}, heat shock proteins {56, 57}, pertussis proteins {58, 59}, protein D from *H.influenzae* {60}, cytokines {61}, lymphokines, hormones, growth factors, toxin A or B from *C.difficile* {62}, iron-uptake proteins {63}, *etc.* Where a mixture comprises capsular saccharides from both serogroups A and C, it may be preferred that the ratio (w/w) of MenA saccharide:MenC saccharide is greater than 1 (*e.g.* 2:1, 3:1, 4:1, 5:1, 10:1 or higher). Different saccharides can be conjugated to the same or different type of carrier protein. Any suitable conjugation reaction can be used, with any suitable linker where necessary.

Toxic protein antigens may be detoxified where necessary *e.g.* detoxification of pertussis toxin by chemical and/or genetic means.

Where a diphtheria antigen is included in the composition it is preferred also to include tetanus antigen and pertussis antigens. Similarly, where a tetanus antigen is included it is preferred also to include diphtheria and pertussis antigens. Similarly, where a pertussis antigen is included it is preferred also to include diphtheria and tetanus antigens.

Antigens in the composition will typically be present at a concentration of at least 1μg/ml each. In general, the concentration of any given antigen will be sufficient to elicit an immune response against that antigen.

As an alternative to using protein antigens in the composition of the invention, nucleic acid encoding the antigen may be used {*e.g.* refs. 64 to 72}. Protein components of the compositions of the invention may thus be replaced by nucleic acid (preferably DNA *e.g.* in the form of a plasmid) that encodes the protein.

Definitions

The term "comprising" means "including" as well as "consisting" *e.g.* a composition "comprising" X may consist exclusively of X or may include something additional *e.g.* X + Y.

The term "about" in relation to a numerical value *x* means, for example, $x \pm 10\%$.

References to a percentage sequence identity between two amino acid sequences means that, when aligned, that percentage of amino acids are the same in comparing the two sequences. This alignment and the percent homology or sequence identity can be determined using software programs known in the art, for example those described in section 7.7.18 of reference 73. A preferred alignment is determined by the Smith-Waterman homology search algorithm using an affine gap search with a gap open penalty of 12 and a gap extension penalty of 2, BLOSUM matrix of 62. The Smith-Waterman homology search algorithm is disclosed in reference 74.

REFERENCES (the contents of which are hereby incorporated by reference)

[1] Tettelin *et al.* (2002) *Proc. Natl. Acad. Sci. USA*, 10.1073/pnas.182380799.

[2] International patent application WO02/34771.

3 Terpe et al., "Overview of tag protein fusions: from molecular and biochemical fundamentals to commercial systems", Appl Microbiol Biotechnol (2003) 60:523 – 533.

4. WO99/27961.

5. WO02/074244.

6. WO02/064162.

7. WO03/028760.

8. Gennaro (2000) *Remington: The Science and Practice of Pharmacy.* 20th ed., ISBN: 0683306472.

9. *Vaccine design:the subunit and adjuvant approach* (1995) Powell & Newman. ISBN 0-306-44867-X.

10. WO00/23105.

11. WO00/07621.

12. Barr, et al., "ISCOMs and other saponin based adjuvants", Advanced Drug Delivery Reviews (1998) 32:247 – 271. See also Sjolander, et al., "Uptake and adjuvant activity of orally delivered saponin and ISCOM vaccines", Advanced Drug Delivery Reviews (1998) 32:321 – 338.

13. Niikura et al., "Chimeric Recombinant Hepatitis E Virus-Like Particles as an Oral Vaccine Vehicle Presenting Foreign Epitopes", Virology (2002) 293:273 – 280.

14. Lenz et al., "Papillomarivurs-Like Particles Induce Acute Activation of Dendritic Cells", Journal of Immunology (2001) 5246 – 5355.

15. Pinto, et al., "Cellular Immune Responses to Human Papillomavirus (HPV)-16 L1 Healthy Volunteers Immunized with Recombinant HPV-16 L1 Virus-Like Particles", Journal of Infectious Diseases (2003) 188:327 – 338.

16. Gerber et al., "Human Papillomavrisu Virus-Like Particles Are Efficient Oral Immunogens when Coadministered with Escherichia coli Heat-Labile Entertoxin Mutant R192G or CpG", Journal of Virology (2001) 75(10):4752 – 4760.

17. Gluck et al., "New Technology Platforms in the Development of Vaccines for the Future", Vaccine (2002) 20:B10 –B16.

18. Johnson *et al.* (1999) *Bioorg Med Chem Lett* 9:2273-2278.

19. Meraldi et al., "OM-174, a New Adjuvant with a Potential for Human Use, Induces a Protective Response with Administered with the Synthetic C-Terminal Fragment 242-310 from the circumsporozoite protein of Plasmodium berghei", Vaccine (2003) 21:2485 – 2491.

20. Pajak, et al., "The Adjuvant OM-174 induces both the migration and maturation of murine dendritic cells in vivo", Vaccine (2003) 21:836 – 842.

21. Kandimalla, et al., "Divergent synthetic nucleotide motif recognition pattern: design and development of potent immunomodulatory oligodeoxyribonucleotide agents with distinct cytokine induction profiles", Nucleic Acids Research (2003) 31(9): 2393 – 2400.

22. Krieg, "CpG motifs: the active ingredient in bacterial extracts?", Nature Medicine (2003) 9(7): 831 – 835.

23. McCluskie, et al., "Parenteral and mucosal prime-boost immunization strategies in mice with hepatitis B surface antigen and CpG DNA", FEMS Immunology and Medical Microbiology (2002) 32:179 – 185.

24. Kandimalla, et al., "Toll-like receptor 9: modulation of recognition and cytokine induction by novel synthetic CpG DNAs", Biochemical Society Transactions (2003) 31 (part 3): 654 – 658.

25. Blackwell, et al., "CpG-A-Induced Monocyte IFN-gamma-Inducible Protein-10 Production is Regulated by Plasmacytoid Dendritic Cell Derived IFN-alpha", J. Immunol. (2003) 170(8):4061 – 4068.

26. Krieg, "From A to Z on CpG", TRENDS in Immunology (2002) 23(2): 64 – 65.

27. Kandimalla, et al., "Secondary structures in CpG oligonucleotides affect immunostimulatory activity", BBRC (2003) 306:948 – 953.

28. Kandimalla, et al., "Toll-like receptor 9: modulation of recognition and cytokine induction by novel synthetic GpG DNAs", Biochemical Society Transactions (2003) 31(part 3):664 – 658.
29. Bhagat et al., "CpG penta- and hexadeoxyribonucleotides as potent immunomodulatory agents" BBRC (2003) 300:853 – 861.
30. Singh *et al.* (2001) *J. Cont. Rele.* 70:267-276.
31. WO99/27960.
32. WO99/52549.
33. WO01/21207.
34. WO01/21152.
35. Andrianov et al., "Preparation of hydrogel microspheres by coacervation of aqueous polyphophazene solutions", Biomaterials (1998) 19(1 – 3):109 – 115.
36. Payne et al., "Protein Release from Polyphosphazene Matrices", Adv. Drug. Delivery Review (1998) 31(3):185 – 196.
37. Stanley, "Imiquimod and the imidazoquinolones: mechanism of action and therapeutic potential" Clin Exp Dermatol (2002) 27(7):571 – 577.
38. Jones, "Resiquimod 3M", Curr Opin Investig Drugs (2003) 4(2):214 – 218.
39. WO99/11241.
40. WO98/57659.
41. European patent applications 0835318, 0735898 and 0761231.
42. Ramsay *et al.* (2001) *Lancet* 357(9251):195-196.
43. Lindberg (1999) *Vaccine* 17 Suppl 2:S28-36.
44. Buttery & Moxon (2000) *J R Coll Physicians Lond* 34:163-168.
45. Ahmad & Chapnick (1999) *Infect Dis Clin North Am* 13:113-133, vii.
46. Goldblatt (1998) *J. Med. Microbiol.* 47:563-567.
47. European patent 0 477 508.
48. US Patent No. 5,306,492.
49. International patent application WO98/42721.
50. *Conjugate Vaccines* (eds. Cruse *et al.*) ISBN 3805549326, particularly vol. 10:48-114.
51. Hermanson (1996) *Bioconjugate Techniques* ISBN: 0123423368 or 012342335X.
52. *Research Disclosure*, 453077 (Jan 2002)
53. EP-A-0372501
54. EP-A-0378881
55. EP-A-0427347
56. WO93/17712
57. WO94/03208
58. WO98/58668
59. EP-A-0471177
60. WO00/56360
61. WO91/01146
62. WO00/61761
63. WO01/72337
64. Robinson & Torres (1997) *Seminars in Immunology* 9:271-283.
65. Donnelly *et al.* (1997) *Annu Rev Immunol* 15:617-648.
66. Scott-Taylor & Dalgleish (2000) *Expert Opin Investig Drugs* 9:471-480.
67. Apostolopoulos & Plebanski (2000) *Curr Opin Mol Ther* 2:441-447.
68. Ilan (1999) *Curr Opin Mol Ther* 1:116-120.
69. Dubensky *et al.* (2000) *Mol Med* 6:723-732.
70. Robinson & Pertmer (2000) *Adv Virus Res* 55:1-74.

71. Donnelly *et al.* (2000) *Am J Respir Crit Care Med* 162(4 Pt 2):S190-193.
72. Davis (1999) *Mt. Sinai J. Med.* 66:84-90.
73. *Current Protocols in Molecular Biology* (F.M. Ausubel *et al.*, eds., 1987) Supplement 30.
74. Smith & Waterman (1981) *Adv. Appl. Math.* 2: 482-489.

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